

## INVENTOR SEARCH

=> fil pascal biotechno wpix biosis dissabs lifesci esbio biotechds bioeng  
scisearch;d que 1126; fil capl; d que 135; fil medl; d que 166; fil embase; d que  
197; dup rem 166,135,1126,197

FILE 'PASCAL' ENTERED AT 10:02:44 ON 30 NOV 2010

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L98	1063	SEA CURTISS R/AU OR CURTISS R III/AU OR CURTISS ROY?/AU
L99	249856	SEA SALMONELLA
L100	8	SEA ((ARACP OR ARA CP) (W) BAD OR ARACPBAD OR ARA CPBAD)
L101	1088	SEA FUR GENE#
L102	1719	SEA FERRIC UPTAKE REGULAT?
L103	13365	SEA O(W) ANTIGEN#
L104	2667600	SEA MUTAT? OR MUTANT#
L105	965	SEA MANNOSE(1A) PHOSPHATE ISOMERASE
L106	5259	SEA PMI OR ΔPMI OR DELTAPMI
L107	83	SEA PFUR? OR DELTAPFUR?
L108	4	SEA TTARA?
L109	751214	SEA ATTENUAT?
L115	89324	SEA OUTER MEMBRANE
L120	100416	SEA L99(W) TYPHIMURIUM
L126	29	SEA L98 AND L120 AND (L104 OR L109) AND (L100 OR L101 OR L102 OR L103 OR L105 OR L106 OR L107 OR L108 OR L115)

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FILE COVERS 1907 - 30 Nov 2010 VOL 153 ISS 23  
 FILE LAST UPDATED: 29 Nov 2010 (20101129/ED)  
 REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2010  
 USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2010

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L2	252	SEA FILE=CAPLUS SPE=ON ABB=ON	CURTISS R/AU OR CURTISS R III/AU OR CURTISS RAY III/AU OR CURTISS ROY?/AU
L3	37998	SEA FILE=CAPLUS SPE=ON ABB=ON	SALMONELLA/CW
L4	3	SEA FILE=CAPLUS SPE=ON ABB=ON	((ARACP OR ARA CP) (W)BAD OR ARACPBAD OR ARA CPBAD)/BI
L5	708	SEA FILE=CAPLUS SPE=ON ABB=ON	GENE#/OBI(L)FUR/OBI OR (FUR GENE#)/BI
L7	51696	SEA FILE=CAPLUS SPE=ON ABB=ON	ATTENUAT?/OBI
L8	10	SEA FILE=CAPLUS SPE=ON ABB=ON	L3 AND L5 AND L7
L9	38618	SEA FILE=CAPLUS SPE=ON ABB=ON	LIPOPOLYSACCHARIDES/CT
L11	524	SEA FILE=CAPLUS SPE=ON ABB=ON	L9(L)SYNTHES?/OBI
L12	1	SEA FILE=CAPLUS SPE=ON ABB=ON	L11 AND L3 AND L5
L15	3376	SEA FILE=CAPLUS SPE=ON ABB=ON	O/OBI(L)ANTIGEN#/CW
L18	2	SEA FILE=CAPLUS SPE=ON ABB=ON	L15 AND L3 AND (L4 OR L5)
L19	3	SEA FILE=CAPLUS SPE=ON ABB=ON	L11 AND L15 AND L3
L21	6	SEA FILE=CAPLUS SPE=ON ABB=ON	L3 AND L7 AND L15 AND L9
L22	970	SEA FILE=CAPLUS SPE=ON ABB=ON	PMI/BI
L23	3	SEA FILE=CAPLUS SPE=ON ABB=ON	PFUR/BI
L28	328337	SEA FILE=CAPLUS SPE=ON ABB=ON	MUTAT?/OBI OR MUTANT#/OBI
L29	18181	SEA FILE=CAPLUS SPE=ON ABB=ON	L3(L)TYPHIMURIUM/OBI
L31	10	SEA FILE=CAPLUS SPE=ON ABB=ON	L22 AND L28 AND L29
L32	9	SEA FILE=CAPLUS SPE=ON ABB=ON	L22 AND L28 AND L29 AND L7
L33	1	SEA FILE=CAPLUS SPE=ON ABB=ON	L31 NOT L32
L35	12	SEA FILE=CAPLUS SPE=ON ABB=ON	L2 AND (L4 OR L8 OR L12 OR L18 OR L19 OR L21 OR L23 OR L33)

FILE 'MEDLINE' ENTERED AT 10:02:44 ON 30 NOV 2010

FILE LAST UPDATED: 27 Nov 2010 (20101127/UP). FILE COVERS 1946 TO DATE.

MEDLINE and LMEDLINE have been updated with the 2010 Medical Subject Headings (MeSH) vocabulary and tree numbers from the U.S. National Library of Medicine (NLM). Additional information is available at

[http://www.nlm.nih.gov/pubs/techbull/nd09/nd09\\_medline\\_data\\_changes\\_2010.html](http://www.nlm.nih.gov/pubs/techbull/nd09/nd09_medline_data_changes_2010.html).

The Medline file has been reloaded effective January 24, 2010. See HELP RLOAD for details.

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See HELP RANGE before carrying out any RANGE search.

L36	248	SEA FILE=MEDLINE	SPE=ON	ABB=ON	CURTISS R?/AU,AUTH
L37	48420	SEA FILE=MEDLINE	SPE=ON	ABB=ON	SALMONELLA+NT/CT
L38	1	SEA FILE=MEDLINE	SPE=ON	ABB=ON	((ARACP OR ARA CP) (W)BAD OR ARACPBAD OR ARA CPBAD)
L39	2584	SEA FILE=MEDLINE	SPE=ON	ABB=ON	O ANTIGENS/CT
L40	7659	SEA FILE=MEDLINE	SPE=ON	ABB=ON	VACCINES, ATTENUATED/CT
L41	491950	SEA FILE=MEDLINE	SPE=ON	ABB=ON	MUTATION+NT/CT
L42	11848	SEA FILE=MEDLINE	SPE=ON	ABB=ON	MUTANT PROTEINS+NT/CT
L43	154	SEA FILE=MEDLINE	SPE=ON	ABB=ON	FUR GENE#
L44	958	SEA FILE=MEDLINE	SPE=ON	ABB=ON	PMI OR ΔPMI
L45	2	SEA FILE=MEDLINE	SPE=ON	ABB=ON	PFUR
L52	490	SEA FILE=MEDLINE	SPE=ON	ABB=ON	FERRIC UPTAKE REGULATING PROTEINS, BACTERIAL/CN
L56	20666	SEA FILE=MEDLINE	SPE=ON	ABB=ON	BACTERIAL OUTER MEMBRANE PROTEINS+NT/CT
L59	262	SEA FILE=MEDLINE	SPE=ON	ABB=ON	MANNOSE-6-PHOSPHATE ISOMERASE/ CT
L66	5	SEA FILE=MEDLINE	SPE=ON	ABB=ON	L36 AND L37 AND (L40 OR L41 OR L42) AND (L38 OR L39 OR L43 OR L44 OR L45 OR L52 OR L56 OR L59)

FILE 'EMBASE' ENTERED AT 10:02:44 ON 30 NOV 2010  
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FILE COVERAGE: EMBASE-originated material 1947 to 26 Nov 2010 (20101126/ED)  
Unique MEDLINE content 1948 to present

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and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L67	19	SEA FILE=EMBASE	SPE=ON	ABB=ON	CURTISS R?/AU
L68	67092	SEA FILE=EMBASE	SPE=ON	ABB=ON	SALMONELLA+NT/CT
L70	367	SEA FILE=EMBASE	SPE=ON	ABB=ON	FERRIC UPTAKE REGULAT?
L71	190	SEA FILE=EMBASE	SPE=ON	ABB=ON	FUR GENE#

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L72      41 SEA FILE=EMBASE SPE=ON  ABB=ON  FUR GENE/CT
L73      325 SEA FILE=EMBASE SPE=ON  ABB=ON  MANNOSE PHOSPHATE ISOMERASE/CT

L74      2711 SEA FILE=EMBASE SPE=ON  ABB=ON  O ANTIGEN/CT
L75      1095 SEA FILE=EMBASE SPE=ON  ABB=ON  PMI OR ΔPMI OR DELTAPMI
L76      4 SEA FILE=EMBASE SPE=ON  ABB=ON  PFUR
L77      3 SEA FILE=EMBASE SPE=ON  ABB=ON  TTARA?
L78      11332 SEA FILE=EMBASE SPE=ON  ABB=ON  LIVE VACCINE/CT
L79      189362 SEA FILE=EMBASE SPE=ON  ABB=ON  ATTENUAT?
L80      544225 SEA FILE=EMBASE SPE=ON  ABB=ON  MUTATION+NT/CT
L81      48065 SEA FILE=EMBASE SPE=ON  ABB=ON  MUTANT/CT OR BACTERIUM
        MUTANT+NT/CT
L82      31722 SEA FILE=EMBASE SPE=ON  ABB=ON  MUTANT PROTEIN/CT
L83      25 SEA FILE=EMBASE SPE=ON  ABB=ON  PFUR?
L84      1 SEA FILE=EMBASE SPE=ON  ABB=ON  ((ARACP OR ARA CP) (W)BAD OR
        ARACPBAD OR ARA CPBAD)
L97      9 SEA FILE=EMBASE SPE=ON  ABB=ON  L67 AND L68 AND (L70 OR L71 OR
        L72 OR L73 OR L74 OR L75 OR L76 OR L77 OR L78 OR L79 OR L80 OR
        L81 OR L82 OR L83 OR L84)

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 PROCESSING COMPLETED FOR L66  
 PROCESSING COMPLETED FOR L35  
 PROCESSING COMPLETED FOR L126  
 PROCESSING COMPLETED FOR L97

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L128      39 DUP REM L66 L35 L126 L97 (16 DUPLICATES REMOVED)
        ANSWERS '1-5' FROM FILE MEDLINE
        ANSWERS '6-14' FROM FILE CAPLUS
        ANSWER '15' FROM FILE PASCAL

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ANSWER '16' FROM FILE WPIX  
 ANSWERS '17-27' FROM FILE BIOSIS  
 ANSWER '28' FROM FILE BIOTECHDS  
 ANSWERS '29-30' FROM FILE SCISEARCH  
 ANSWERS '31-39' FROM FILE EMBASE

=> d iall 1-5; d ibib abs hitind 6-14; d iall 15; d ifull 16; d iall 17-39

L128 ANSWER 1 OF 39 MEDLINE on STN DUPLICATE 1  
 ACCESSION NUMBER: 2009757622 MEDLINE Full-text  
 DOCUMENT NUMBER: PubMed ID: 19805538  
 TITLE: Regulated delayed expression of rfaH in an attenuated  
 Salmonella enterica serovar typhimurium vaccine enhances  
 immunogenicity of outer membrane proteins and a  
 heterologous antigen.  
 AUTHOR: Kong Qingke; Liu Qing; Roland Kenneth L; Curtiss Roy  
 3rd  
 CORPORATE SOURCE: Center for Infectious Diseases and Vaccinology, The  
 Biodesign Institute, Arizona State University, PO Box  
 875401, Tempe, Arizona 85287-5401, USA.  
 SOURCE: Infection and immunity, (2009 Dec) Vol. 77, No. 12, pp.  
 5572-82. Electronic Publication: 2009-10-05.  
 Journal code: 0246127. E-ISSN: 1098-5522. L-ISSN:  
 0019-9567.  
 Report No.: NLM-PMC2786485.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200912  
 ENTRY DATE: Entered STN: 17 Nov 2009  
 Last Updated on STN: 16 Dec 2009  
 Entered Medline: 4 Dec 2009  
 ABSTRACT:  
 RfaH is a transcriptional antiterminator that reduces the polarity of long  
 operons encoding secreted and surface-associated cell components of Salmonella  
 enterica serovar Typhimurium, including O antigen and lipopolysaccharide core  
 sugars. A DeltarfaH mutant strain is attenuated in mice (50% lethal dose  
 [LD(50)], >10(8) CFU). To examine the potential for using rfaH in conjunction  
 with other attenuating mutations, we designed a series of strains in which we  
 replaced the native rfaH promoter with the tightly regulated  
 arabinose-dependent araC P(BAD) promoter so that rfaH expression was dependent  
 on exogenously supplied arabinose provided during in vitro growth. Following  
 colonization of host lymphoid tissues, where arabinose was not available, the  
 P(BAD) promoter was no longer active and rfaH was not expressed. In the  
 absence of RfaH, O antigen and core sugars were not synthesized. We  
 constructed three mutant strains that expressed different levels of RfaH by  
 altering the ribosome-binding sequence and start codon. One mutation,  
 DeltaP(rfaH178), was introduced into the attenuated vaccine strain chi9241  
 (DeltapabA DeltapabB DeltaasdA) expressing the pneumococcal surface protein  
 PspA from an Asd(+) balanced-lethal plasmid. Mice immunized with this strain  
 and boosted 4 weeks later induced higher levels of serum immunoglobulin G  
 specific for PspA and for outer membrane proteins from other enteric bacteria  
 than either an isogenic DeltarfaH derivative or the isogenic RfaH(+) parent.  
 Eight weeks after primary oral immunization, mice were challenged with 200  
 LD(50) of virulent Streptococcus pneumoniae WU2. Immunization with  
 DeltaP(rfaH178) mutant strains led to increased levels of protection compared  
 to that of the parent chi9241 and of a DeltarfaH derivative of chi9241.  
 CONTROLLED TERM: Check Tags: Female

Animals  
 Antibodies, Bacterial: BL, blood  
 Antigens, Heterophile: GE, genetics  
 \*Antigens, Heterophile: IM, immunology  
 Arabinose: ME, metabolism  
     Bacterial Outer Membrane Proteins: GE, genetics  
     \*Bacterial Outer Membrane Proteins: IM, immunology  
 \*Bacterial Proteins: BI, biosynthesis  
     Bacterial Proteins: GE, genetics  
     Bacterial Proteins: IM, immunology  
     Gene Deletion  
 \*Gene Expression Regulation, Bacterial  
     Immunization, Secondary: MT, methods  
     Immunoglobulin G: BL, blood  
 Mice  
     Mice, Inbred BALB C  
     Pneumococcal Infections: PC, prevention & control  
     Promoter Regions, Genetic  
     Salmonella Vaccines: GE, genetics  
 \*Salmonella Vaccines: IM, immunology  
     Salmonella typhimurium: GE, genetics  
     \*Salmonella typhimurium: IM, immunology  
     Streptococcus pneumoniae: IM, immunology  
 Survival Analysis  
 Transcriptional Activation  
     Vaccines, Attenuated: GE, genetics  
     Vaccines, Attenuated: IM, immunology

CAS REGISTRY NO.: 147-81-9 (Arabinose)

CHEMICAL NAME: 0 (Antibodies, Bacterial); 0 (Antigens, Heterophile); 0  
 (Bacterial Outer Membrane Proteins); 0 (Bacterial  
 Proteins); 0 (Immunoglobulin G); 0 (Salmonella Vaccines); 0  
 (Vaccines, Attenuated); 0 (pneumococcal surface protein A)

MEDLINE REFERENCE COUNT: 44 There are 44 cited references available in  
 MEDLINE for this document.

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L128 ANSWER 2 OF 39            MEDLINE on STN            DUPLICATE 2

ACCESSION NUMBER:    2009145883            MEDLINE    Full-text

DOCUMENT NUMBER:    PubMed ID: 19103774

TITLE:                Salmonella enterica serovar typhimurium strains with  
regulated delayed attenuation in vivo.

AUTHOR:               Curtiss Roy 3rd; Wanda Soo-Young; Gunn Bronwyn M;  
Zhang Xin; Tinge Steven A; Ananthnarayan Vidya; Mo Hua;  
Wang Shifeng; Kong Wei

CORPORATE SOURCE:    Center for Infectious Diseases and Vaccinology, Biodesign  
Institute and School of Life Sciences, Arizona State  
University, Tempe, Arizona 85287-5401, USA.  
rcurtiss@asu.edu

CONTRACT NUMBER:    AI056289 (United States NIAID NIH HHS)  
AI24533 (United States NIAID NIH HHS)  
DE06669 (United States NIDCR NIH HHS)

SOURCE:              Infection and immunity, (2009 Mar) Vol. 77, No. 3, pp.  
1071-82.    Electronic Publication: 2008-12-22.  
Journal code: 0246127. E-ISSN: 1098-5522. L-ISSN:  
0019-9567.  
Report No.: NLM-PMC2643627.

PUB. COUNTRY:        United States

DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)

LANGUAGE:            English

FILE SEGMENT:        Priority Journals

ENTRY MONTH:         200903

ENTRY DATE:          Entered STN: 24 Feb 2009  
Last Updated on STN: 20 Mar 2009  
Entered Medline: 19 Mar 2009

## ABSTRACT:

Recombinant bacterial vaccines must be fully attenuated for animal or human hosts to avoid inducing disease symptoms while exhibiting a high degree of immunogenicity. Unfortunately, many well-studied means for attenuating

Salmonella render strains more susceptible to host defense stresses encountered following oral vaccination than wild-type virulent strains and/or impair their ability to effectively colonize the gut-associated and internal lymphoid tissues. This thus impairs the ability of recombinant vaccines to serve as factories to produce recombinant antigens to induce the desired protective immunity. To address these problems, we designed strains that display features of wild-type virulent strains of Salmonella at the time of immunization to enable strains first to effectively colonize lymphoid tissues and then to exhibit a regulated delayed attenuation in vivo to preclude inducing disease symptoms. We recently described one means to achieve this based on a reversible smooth-rough synthesis of lipopolysaccharide O antigen. We report here a second means to achieve regulated delayed attenuation in vivo that is based on the substitution of a tightly regulated araC P(BAD) cassette for the promoters of the fur, crp, phoPQ, and rpoS genes such that expression of these genes is dependent on arabinose provided during growth. Thus, following colonization of lymphoid tissues, the Fur, Crp, PhoPQ, and/or RpoS proteins cease to be synthesized due to the absence of arabinose such that attenuation is gradually manifest in vivo to preclude induction of diseases symptoms. Means for achieving regulated delayed attenuation can be combined with other mutations, which together may yield safe efficacious recombinant attenuated Salmonella vaccines.

CONTROLLED TERM: Check Tags: Female

Animals

Bacterial Outer Membrane Proteins: BI,  
biosynthesis

Bacterial Outer Membrane Proteins: GE, genetics

Bacterial Proteins: BI, biosynthesis

Bacterial Proteins: GE, genetics

Gene Expression

\*Gene Expression Regulation, Bacterial: GE, genetics

Genes, araC: GE, genetics

Mice

Mice, Inbred BALB C

Mice, Inbred C57BL

Mutation

Phenotype

Promoter Regions, Genetic

Repressor Proteins: BI, biosynthesis

Repressor Proteins: GE, genetics

\*Salmonella Vaccines: IM, immunology

\*Salmonella typhimurium: GE, genetics

Salmonella typhimurium: IM, immunology

\*Salmonella typhimurium: PY, pathogenicity

Sigma Factor: BI, biosynthesis

Sigma Factor: GE, genetics

Vaccines, Attenuated

Virulence

CHEMICAL NAME: 0 (Bacterial Outer Membrane Proteins); 0 (Bacterial Proteins); 0 (Omp2 protein, bacteria); 0 (PhoQ protein, Bacteria); 0 (Repressor Proteins); 0 (Salmonella Vaccines); 0 (Sigma Factor); 0 (Vaccines, Attenuated); 0 (ferric uptake regulating proteins, bacterial); 0 (sigma factor KatF protein, Bacteria)

MEDLINE REFERENCE COUNT: 73 There are 73 cited references available in MEDLINE for this document.

REFERENCE(S): CITED REFERENCES AVAILABLE IN MEDLINE

- (1) Hengge-Aronis, R; Mol Microbiol. 1992 Jul, V6(14), P1877-86. MEDLINE
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L128 ANSWER 3 OF 39 MEDLINE on STN DUPLICATE 4  
 ACCESSION NUMBER: 2007114809 MEDLINE Full-text  
 DOCUMENT NUMBER: PubMed ID: 17178790  
 TITLE: Role of RpoS in fine-tuning the synthesis of Vi capsular polysaccharide in Salmonella enterica serotype Typhi.  
 AUTHOR: Santander Javier; Wanda Soo-Young; Nickerson Cheryl A; Curtiss Roy 3rd  
 CORPORATE SOURCE: The Biodesign Institute, Center for Infectious Diseases and Vaccinology, Arizona State University, PO Box 875401, 1001 S. McAllister Avenue, Tempe, AZ 85287-5401, USA.  
 CONTRACT NUMBER: R01 AI056289 (United States NIAID NIH HHS)  
 R01 AI057885 (United States NIAID NIH HHS)  
 R01 AI24533 (United States NIAID NIH HHS)  
 SOURCE: Infection and immunity, (2007 Mar) Vol. 75, No. 3, pp. 1382-92. Electronic Publication: 2006-12-18.  
 Journal code: 0246127. ISSN: 0019-9567. L-ISSN: 0019-9567.  
 Report No.: NLM-PMC1828562.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, N.I.H., EXTRAMURAL)  
 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200704  
 ENTRY DATE: Entered STN: 27 Feb 2007  
 Last Updated on STN: 11 Apr 2007  
 Entered Medline: 10 Apr 2007

## ABSTRACT:

Regulation of the synthesis of Vi polysaccharide, a major virulence determinant in Salmonella enterica serotype Typhi, is under the control of two regulatory systems, ompR-envZ and rscB-rscC, which respond to changes in osmolarity. Some serotype Typhi strains exhibit overexpression of Vi polysaccharide, which masks clinical detection of lipopolysaccharide O antigen. This variation in Vi polysaccharide and O antigen display (VW variation) has been observed since the initial studies of serotype Typhi. In this study, we report that rpoS plays a role in this increased expression in Vi polysaccharide. We constructed a variety of isogenic serotype Typhi mutants that differed in their expression levels of RpoS and examined the role of the rpoS product in synthesis of Vi polysaccharide under different osmolarity conditions. Vi polysaccharide synthesis was also examined in serotype Typhi mutants in which the native promoter of the rpoS was replaced by an araCP(BAD) cassette, so that the expression of rpoS was arabinose dependent. The RpoS(-) strains showed increased syntheses of Vi polysaccharide, which at low and medium osmolarities masked O antigen detection. In contrast, RpoS(+) strains

showed lower syntheses of Vi polysaccharide, and an increased detection of O antigen was observed. During exponential growth, when *rpoS* is unstable or present at low levels, serotype Typhi RpoS(+) strains overexpress the Vi polysaccharide at levels comparable to those for RpoS(-) strains. Our results show that RpoS is another regulator of Vi polysaccharide synthesis and contributes to VW variation in serotype Typhi, which has implications for the development of recombinant attenuated *Salmonella* vaccines in humans.

CONTROLLED TERM: \*Bacterial Proteins: PH, physiology

Drug Design

O Antigens: ME, metabolism

\*Polysaccharides, Bacterial: BI, biosynthesis

Polysaccharides, Bacterial: GE, genetics

*Salmonella typhi*: GE, genetics

*Salmonella typhi*: IM, immunology

\**Salmonella typhi*: ME, metabolism

\*Sigma Factor: PH, physiology

Vaccines, Attenuated: CS, chemical synthesis

Vaccines, Attenuated: GE, genetics

Vaccines, Synthetic: CH, chemistry

Vaccines, Synthetic: GE, genetics

CHEMICAL NAME: 0 (Bacterial Proteins); 0 (O Antigens); 0 (Polysaccharides, Bacterial); 0 (Sigma Factor); 0 (Vaccines, Attenuated); 0 (Vaccines, Synthetic); 0 (capsular polysaccharide, *Salmonella*); 0 (sigma factor KatF protein, Bacteria)

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L128 ANSWER 4 OF 39 MEDLINE on STN

ACCESSION NUMBER: 1999386855 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 10456909

TITLE: Attenuation and immunogenicity of Deltacya Deltacrp derivatives of Salmonella choleraesuis in pigs.

AUTHOR: Kennedy M J; Yancey R J Jr; Sanchez M S; Rzepkowski R A; Kelly S M; Curtiss R 3rd

CORPORATE SOURCE: Animal Health Discovery Research, Veterinary Infectious Diseases Section, Pharmacia & Upjohn, Inc., Kalamazoo, Michigan 49001, USA.. Michael.J.Kennedy@am.pnu.com

SOURCE: Infection and immunity, (1999 Sep) Vol. 67, No. 9, pp. 4628-36.  
Journal code: 0246127. ISSN: 0019-9567. L-ISSN: 0019-9567.  
Report No.: NLM-PMC96787.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199910

ENTRY DATE: Entered STN: 14 Oct 1999



Last Updated on STN: 14 Oct 1999  
Entered Medline: 5 Oct 1999

## ABSTRACT:

Six different isogenic Deltacya Deltacrp derivatives of a strain of *Salmonella choleraesuis* var. *kunzendorf-chi3246* virulent for pigs were constructed by transposon-mediated deletion mutagenesis. These strains were evaluated for virulence and ability to elicit a protective immune response in young weaned pigs after oral administration and were compared to a commercially available vaccine which lacks the 50-kb virulence plasmid (vpl(-)). These derivatives were Deltacya Deltacrp vpl(+), Deltacya Deltacrp vpl(-), Deltacya Delta(crp-cdt) vpl(+), Deltacya Delta(crp-cdt) vpl(-), Deltacya Deltacrp \*\*\*pmi\*\*\* -3834 vpl(+), and Deltacya Delta(crp-cdt) pmi-3834. In experiments to evaluate safety, no significant adverse effects of any of the vaccine constructs were observed, except that two of the strains which carried the virulence plasmid (vpl(+)) caused a small, short-term elevation in maximum temperature compared to pretreatment temperature values. Orally immunized animals, except for those vaccinated with the Deltacya Deltacrp pmi-3834 vpl(+) strain or SC-54, developed significant serum antibody responses 21 days postvaccination as measured by enzyme-linked immunosorbent assay. No cell-mediated immune responses to heat-killed *S. choleraesuis* were noted at the same time point as measured with heat-killed bacteria as antigen in a lymphocyte proliferation assay. In an oral challenge exposure model with a highly virulent heterologous strain of *S. choleraesuis*, the Deltacya Deltacrp strains with deletions in pmi were not protective. As measured by morbidity scores, the responses to challenge of the pigs vaccinated with the other four Deltacya Deltacrp derivatives were significantly better than those of the nonvaccinated, challenged group. With the exception of temperature elevation and slight differences in diarrhea scores postchallenge, none of these strains differed significantly from each other in the other clinical parameters analyzed. While the commercial vaccine was protective by most of the parameters measured, it was not fully protective against challenge with virulent *S. choleraesuis* as judged by diarrhea scores and temperature elevation. Collectively, these data demonstrate that Deltacya Deltacrp derivatives, with or without the virulence plasmid but not with deletions in the pmi gene, are candidates for vaccines for protection against salmonellosis in pigs.

CONTROLLED TERM: Check Tags: Female; Male  
Animals  
Antibodies, Bacterial: BL, blood  
Antibodies, Bacterial: IM, immunology  
Bacterial Vaccines: GE, genetics  
\*Bacterial Vaccines: IM, immunology  
Carrier Proteins  
Cyclic AMP: GE, genetics  
\*Cyclic AMP Receptor Protein: GE, genetics  
Mutation  
Salmonella: GE, genetics  
\*Salmonella: IM, immunology  
Salmonella Infections: IM, immunology  
Salmonella Infections: MI, microbiology  
Salmonella Infections: PA, pathology  
Salmonella Infections: PC, prevention & control  
Swine  
Vaccines, Attenuated

CAS REGISTRY NO.: 60-92-4 (Cyclic AMP)

CHEMICAL NAME: 0 (Antibodies, Bacterial); 0 (Bacterial Vaccines); 0 (Carrier Proteins); 0 (Cyclic AMP Receptor Protein); 0 (Vaccines, Attenuated)

MEDLINE REFERENCE COUNT: 39 There are 39 cited references available in MEDLINE for this document.

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L128 ANSWER 5 OF 39 MEDLINE on STN

ACCESSION NUMBER: 1998084503 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 9423887

TITLE: Virulence of a Salmonella typhimurium OmpD mutant.

AUTHOR: Meyer P N; Wilmes-Riesenberg M R; Stathopoulos C; Curtiss R 3rd

CORPORATE SOURCE: Department of Biology, Washington University, St. Louis, Missouri 63130, USA.

SOURCE: Infection and immunity, (1998 Jan) Vol. 66, No. 1, pp. 387-90.

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 ENTRY MONTH: 199801  
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 Entered Medline: 27 Jan 1998

## ABSTRACT:

An ompD mutation caused by a Tn10 insertion was transduced into Salmonella typhimurium SL1344 and UK-1. The adherence and invasion capabilities of the resultant ompD mutants were examined by tissue culture analysis. The virulence of the S. typhimurium ompD mutants was ascertained by a 50% lethal dose (LD50) study and by determining colonization ability with BALB/c mice. We found no statistically significant difference in adherence and invasion capacities between the S. typhimurium wild type strains and their corresponding ompD mutants. Furthermore, the LD50 and colonization studies revealed that there is no statistically significant difference in virulence between the S. typhimurium wild type strains and their corresponding ompD mutants. These results differ from those reported previously (C. J. Dorman, S. Chatfield, C. F. Higgins, C. Hayward, and G. Dougan, Infect. Immun. 57:2136-2140, 1989).

CONTROLLED TERM: Check Tags: Female

Animals

\*Bacterial Outer Membrane Proteins: GE, genetics

Bacterial Outer Membrane Proteins: ME, metabolism

Cells, Cultured

DNA Transposable Elements

Mice

Mice, Inbred BALB C

Mutagenesis, Insertional

\*Salmonella Infections, Animal: GE, genetics

Salmonella Infections, Animal: MI, microbiology

\*Salmonella typhimurium: GE, genetics

\*Salmonella typhimurium: PY, pathogenicity

Virulence: GE, genetics

CHEMICAL NAME: 0 (Bacterial Outer Membrane Proteins); 0 (DNA Transposable Elements)

MEDLINE REFERENCE COUNT: 17 There are 17 cited references available in MEDLINE for this document.

## REFERENCE(S): CITED REFERENCES AVAILABLE IN MEDLINE

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ACCESSION NUMBER: 2002:575217 CAPLUS Full-text  
 DOCUMENT NUMBER: 137:137500  
 TITLE: Attenuation of microorganisms for vaccines  
 by generation of cell wall biosynthesis mutants  
 complemented by an episomal wild-type gene  
 INVENTOR(S): Curtiss, Roy, III  
 PATENT ASSIGNEE(S): Washington University, USA  
 SOURCE: PCT Int. Appl., 86 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002059292	A2	20020801	WO 2001-US42527	20011005
WO 2002059292	A3	20030731		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 6872547	B1	20050329	US 2000-686499	20001011
AU 2002246498	A1	20020806	AU 2002-246498	20011005
EP 1349925	A2	20031008	EP 2001-994067	20011005
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.:			US 2000-686499	A 20001011
			WO 2001-US42527	W 20011005

# ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB A method of maintaining a foreign gene in a microbial population without the need for antibiotic selection and that can be used to attenuate pathogenic microorganisms for vaccine use is described. The methods use microbial host cells that have an inactivating mutation in an essential gene encoding an enzyme which catalyzes a step in the biosynthesis of diaminopimelic acid (DAP). Diaminopimelic acid is essential for cell wall biosynthesis and is not found free in mammals. The mutation therefore cannot be repaired by syntrophism. The cells also have an extrachromosomal vector that includes the complementing gene as a selectable marker and a gene of interest. The vector can integrate into the host cell at the gene carrying the mutation leading to the diaminopimelic acid auxotrophy. This stabilizes the foreign gene in the host. Expression of the complementing gene is kept to the min. compatible with survival of the host to maintain pressure that prevents excision of the transgene. The cells of the invention are particularly useful for the manufacture of antigens for use in vaccines, including DNA vaccines. A series of expts. with the asd gene of Salmonella typhimurium that demonstrate the practice of the invention are reported. IPCI C12N0015-00 [ICM, 7]

IPCR A61K0039-00 [I,C\*]; A61K0039-00 [I,A]; A61K0039-02 [I,C\*]; A61K0039-02 [I,A]; A61K0039-112 [I,C\*]; A61K0039-112 [I,A]; A61K0048-00 [I,C\*]; A61K0048-00 [I,A]; C07K0014-195 [I,C\*]; C07K0014-24 [I,A]; C12N0015-70 [I,C\*]; C12N0015-70 [I,A]; C12N0015-74 [I,C\*]; C12N0015-74 [I,A]

CC 10-4 (Microbial, Algal, and Fungal Biochemistry)

Section cross-reference(s): 15

ST attenuation mutation complementation transgene integration  
 stabilization; cell wall biosynthesis mutation attenuation

vaccine

IT Animal virus  
Eubacteria  
Gamete and Germ cell  
Parasite  
(antigens of, manufacture in attenuated bacterial host;  
attenuation of microorganisms for vaccines by generation of  
cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(aro, as essential gene, attenuation by mutation in;  
attenuation of microorganisms for vaccines by generation of  
cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(aroA, as essential gene, attenuation by mutation in;  
attenuation of microorganisms for vaccines by generation of  
cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(aroC, as essential gene, attenuation by mutation in;  
attenuation of microorganisms for vaccines by generation of  
cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(asd, mutations in; attenuation of microorganisms for  
vaccines by generation of cell wall biosynthesis mutants complemented  
by episomal wild-type gene)

IT Enterobacteriaceae  
Pathogen  
Virulence (microbial)  
(attenuation of; attenuation of microorganisms for  
vaccines by generation of cell wall biosynthesis mutants complemented  
by episomal wild-type gene)

IT Egg  
Sperm  
(autoantigens of, manufacture in attenuated bacterial host;  
attenuation of microorganisms for vaccines by generation of  
cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Antigens  
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL  
(Biological study); PREP (Preparation); USES (Uses)  
(autoantigens, manufacture in attenuated bacterial host;  
attenuation of microorganisms for vaccines by generation of  
cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(cdt, as essential gene, attenuation by mutation in;  
attenuation of microorganisms for vaccines by generation of  
cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Salmonella typhimurium  
(cell wall mutants and attenuation of; attenuation  
of microorganisms for vaccines by generation of cell wall biosynthesis  
mutants complemented by episomal wild-type gene)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)  
 (crp, as essential gene, attenuation by mutation in;  
 attenuation of microorganisms for vaccines by generation of  
 cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (cya, as essential gene, attenuation by mutation in;  
 attenuation of microorganisms for vaccines by generation of  
 cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (dam, as essential gene, attenuation by mutation in;  
 attenuation of microorganisms for vaccines by generation of  
 cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (dap, mutations in; attenuation of microorganisms for  
 vaccines by generation of cell wall biosynthesis mutants complemented  
 by episomal wild-type gene)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (dapA, as essential gene, attenuation by mutation in;  
 attenuation of microorganisms for vaccines by generation of  
 cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (dapB, as essential gene, attenuation by mutation in;  
 attenuation of microorganisms for vaccines by generation of  
 cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (dapD, as essential gene, attenuation by mutation in;  
 attenuation of microorganisms for vaccines by generation of  
 cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (dapE, as essential gene, attenuation by mutation in;  
 attenuation of microorganisms for vaccines by generation of  
 cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (dapF, as essential gene, attenuation by mutation in;  
 attenuation of microorganisms for vaccines by generation of  
 cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Mutation  
 (deletion, for inactivation of essential genes; attenuation  
 of microorganisms for vaccines by generation of cell wall biosynthesis  
 mutants complemented by episomal wild-type gene)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (flgM, as essential gene, attenuation by mutation in;  
 attenuation of microorganisms for vaccines by generation of

- cell wall biosynthesis mutants complemented by episomal wild-type gene)
- IT Plasmid vectors  
(for attenuation of bacteria; attenuation of microorganisms for vaccines by generation of cell wall biosynthesis mutants complemented by episomal wild-type gene)
- IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(fur, as essential gene, attenuation by mutation in; attenuation of microorganisms for vaccines by generation of cell wall biosynthesis mutants complemented by episomal wild-type gene)
- IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(galeE, as essential gene, attenuation by mutation in; attenuation of microorganisms for vaccines by generation of cell wall biosynthesis mutants complemented by episomal wild-type gene)
- IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(galU, as essential gene, attenuation by mutation in; attenuation of microorganisms for vaccines by generation of cell wall biosynthesis mutants complemented by episomal wild-type gene)
- IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(hemA, as essential gene, attenuation by mutation in; attenuation of microorganisms for vaccines by generation of cell wall biosynthesis mutants complemented by episomal wild-type gene)
- IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(hila, as essential gene, attenuation by mutation in; attenuation of microorganisms for vaccines by generation of cell wall biosynthesis mutants complemented by episomal wild-type gene)
- IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(htrA, as essential gene, attenuation by mutation in; attenuation of microorganisms for vaccines by generation of cell wall biosynthesis mutants complemented by episomal wild-type gene)
- IT Mutation  
(insertion, for inactivation of essential genes; attenuation of microorganisms for vaccines by generation of cell wall biosynthesis mutants complemented by episomal wild-type gene)
- IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(inv, as essential gene, attenuation by mutation in; attenuation of microorganisms for vaccines by generation of cell wall biosynthesis mutants complemented by episomal wild-type gene)
- IT Vaccines  
(live, attenuation of microorganisms for; attenuation of microorganisms for vaccines by generation of cell wall biosynthesis mutants complemented by episomal wild-type gene)
- IT Allergens  
Antigens  
Cytokines  
Lymphokines

Tumor antigens

RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(manufacture in attenuated bacterial host; attenuation of microorganisms for vaccines by generation of cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Cell wall

(mutations affecting biosynthesis of; attenuation of microorganisms for vaccines by generation of cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(mviA, as essential gene, attenuation by mutation in; attenuation of microorganisms for vaccines by generation of cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(nadA, as essential gene, attenuation by mutation in; attenuation of microorganisms for vaccines by generation of cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Promoter (genetic element)

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(of essential gene, minimizing function of, in attenuation of pathogenic bacteria; attenuation of microorganisms for vaccines by generation of cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(ompR, as essential gene, attenuation by mutation in; attenuation of microorganisms for vaccines by generation of cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pab, as essential gene, attenuation by mutation in; attenuation of microorganisms for vaccines by generation of cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(phoP, as essential gene, attenuation by mutation in; attenuation of microorganisms for vaccines by generation of cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(phoQ, as essential gene, attenuation by mutation in; attenuation of microorganisms for vaccines by generation of cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pmi, as essential gene, attenuation by mutation in; attenuation of microorganisms for vaccines by generation of cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial



RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(pncB, as essential gene, attenuation by mutation in;  
attenuation of microorganisms for vaccines by generation of  
cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(poxA, as essential gene, attenuation by mutation in;  
attenuation of microorganisms for vaccines by generation of  
cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Cytomegalovirus  
(promoters of, expression of therapeutic gene from; attenuation  
of microorganisms for vaccines by generation of cell wall biosynthesis  
mutants complemented by episomal wild-type gene)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(pur, as essential gene, attenuation by mutation in;  
attenuation of microorganisms for vaccines by generation of  
cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(recA, as essential gene, attenuation by mutation in;  
attenuation of microorganisms for vaccines by generation of  
cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(rfc, as essential gene, attenuation by mutation in;  
attenuation of microorganisms for vaccines by generation of  
cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(rpoE, as essential gene, attenuation by mutation in;  
attenuation of microorganisms for vaccines by generation of  
cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(rpsL, as essential gene, attenuation by mutation in;  
attenuation of microorganisms for vaccines by generation of  
cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(sirA, as essential gene, attenuation by mutation in;  
attenuation of microorganisms for vaccines by generation of  
cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(slyA, as essential gene, attenuation by mutation in;  
attenuation of microorganisms for vaccines by generation of  
cell wall biosynthesis mutants complemented by episomal wild-type gene)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

- (sodC, as essential gene, attenuation by mutation in;  
attenuation of microorganisms for vaccines by generation of  
cell wall biosynthesis mutants complemented by episomal wild-type gene)
- IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(ssrA, as essential gene, attenuation by mutation in;  
attenuation of microorganisms for vaccines by generation of  
cell wall biosynthesis mutants complemented by episomal wild-type gene)
- IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(tonB, as essential gene, attenuation by mutation in;  
attenuation of microorganisms for vaccines by generation of  
cell wall biosynthesis mutants complemented by episomal wild-type gene)
- IT Fungi  
(zoopathogenic, antigens of, manufacture in attenuated bacterial  
host; attenuation of microorganisms for vaccines by  
generation of cell wall biosynthesis mutants complemented by episomal  
wild-type gene)
- IT 444272-82-6  
RL: PRP (Properties)  
(attenuation of microorganisms for vaccines by generation of  
cell wall biosynthesis mutants complemented by an episomal wild-type  
gene)
- IT 583-93-7, Diaminopimelic acid  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(mutations affecting biosynthesis of; attenuation of  
microorganisms for vaccines by generation of cell wall biosynthesis  
mutants complemented by episomal wild-type gene)
- IT 444272-86-0, 4: PN: WO02059292 SEQID: 7 unclaimed DNA 444272-87-1, 5:  
PN: WO02059292 SEQID: 8 unclaimed DNA 444388-50-5, 1: PN: WO02059292  
SEQID: 3 unclaimed DNA  
RL: PRP (Properties)  
(unclaimed nucleotide sequence; attenuation of microorganisms  
for vaccines by generation of cell wall biosynthesis mutants  
complemented by an episomal wild-type gene)
- IT 444272-83-7 444272-84-8 444272-85-9  
RL: PRP (Properties)  
(unclaimed protein sequence; attenuation of microorganisms  
for vaccines by generation of cell wall biosynthesis mutants  
complemented by an episomal wild-type gene)
- IT 444168-40-5 444272-81-5  
RL: PRP (Properties)  
(unclaimed sequence; attenuation of microorganisms for  
vaccines by generation of cell wall biosynthesis mutants complemented  
by an episomal wild-type gene)

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD  
(2 CITINGS)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L128 ANSWER 7 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN DUPLICATE 7

ACCESSION NUMBER: 2002:293472 CAPLUS Full-text

DOCUMENT NUMBER: 136:324050

TITLE: Microbes attenuated by inserting a  
transcription terminator are useful as vaccine or  
carrier for delivering a desired antigen

INVENTOR(S): Curtiss, Roy, III; Tinge, Steven A.

PATENT ASSIGNEE(S): Washington University, USA; Megan Health, Inc.

SOURCE: PCT Int. Appl., 91 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030457	A2	20020418	WO 2001-US31606	20011011
WO 2002030457	A3	20030123		
WO 2002030457	A9	20030724		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2002011582	A	20020422	AU 2002-11582	20011011
CA 2463482	A1	20030418	CA 2001-2463482	20011011
EP 1326960	A2	20030716	EP 2001-979646	20011011
EP 1326960	B1	20041208		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
AT 284440	T	20041215	AT 2001-979646	20011011
PRIORITY APPLN. INFO.:			US 2000-689123	A 20001012
			WO 2001-US31606	W 20011011

AB Compsns. comprising a microbe having an attenuating mutation comprising a recombinant transcription terminator insertion in a chromosomal gene are disclosed. The transcription terminator is rrnB 5s rRNA T1T2, trpA, T4 gene 32, T4 ipIII gene, or rrfG 5S rRNA. The chromosomal gene is pab, pur, aro, asd, dap, nadA, pncB, gale, pmi, fur, rpsL, ompR, htrA, hemA, cdt, cya, crp, phoP, rfc, poxR or galU gene. The microbe is Salmonella, Shigella, Escherichia or hybrid thereof. The compsns. can be used as vaccines or carrier vehicles for delivering a desired protein to an individual. Also disclosed are methods for immunizing an individual and methods of delivering a desired gene product to an individual based upon administration of the compsns.

IPC1 A61K0039-02 [ICM,7]; A61K0039-108 [ICS,7]; A61K0039-112 [ICS,7]  
 IPCR A61K0039-00 [I,C\*]; A61K0039-00 [I,A]; A61P0037-00 [I,C\*]; A61P0037-02 [I,A]; C12N0015-74 [I,C\*]; C12N0015-74 [I,A]

CC 15-2 (Immunochimistry)

Section cross-reference(s): 3, 10, 63

ST attenuated microbe transcription terminator vaccine carrier

IT Gene, microbial

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)

(32, transcription terminator; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)

IT rRNA

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)

(5 S, rrnB 5s rRNA T1T2 transcription terminator; microbes attenuated by inserting a transcription terminator are useful

- as vaccine or carrier for delivering a desired antigen)
- IT Gamete and Germ cell  
(antigen; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Gene, microbial  
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
(aro; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Gene, microbial  
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
(asd; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Antigens  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(autoantigens; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Drug delivery systems  
(carriers; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Gene, microbial  
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
(cdt; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Gene, microbial  
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
(crp; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Gene, microbial  
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
(cya; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Gene, microbial  
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
(dap; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Gene, microbial  
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
(deletion; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Gene, microbial  
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)

- (fur; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
 (galE; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
 (galU; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Antigens  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (gamete-specific; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Coliphage T4  
 (gene 32 transcription terminator; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Chromosome  
 (gene; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
 (hemA; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
 (htrA; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Gene, microbial  
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (ipIII; transcription terminator; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT DNA sequences  
 Drug delivery systems  
 Escherichia  
 Escherichia coli  
 Eubacteria  
 Fungi  
 Immunostimulation  
 Immunosuppression  
 Microorganism  
 Molecular cloning  
 Mutation  
 Parasite

Pathogen  
 Protozoa  
 RNA sequences  
   Salmonella  
 Shigella  
 Vaccines  
 Virus

(microbes attenuated by inserting a transcription terminator  
 are useful as vaccine or carrier for delivering a desired antigen)

IT Promoter (genetic element)

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(microbes attenuated by inserting a transcription terminator  
 are useful as vaccine or carrier for delivering a desired antigen)

IT Allergens

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)

(microbes attenuated by inserting a transcription terminator  
 are useful as vaccine or carrier for delivering a desired antigen)

IT Gene, microbial

RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)

(nadA; microbes attenuated by inserting a transcription  
 terminator are useful as vaccine or carrier for delivering a desired  
 antigen)

IT Gene, microbial

RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)

(ompR; microbes attenuated by inserting a transcription  
 terminator are useful as vaccine or carrier for delivering a desired  
 antigen)

IT Gene, microbial

RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)

(pab; microbes attenuated by inserting a transcription  
 terminator are useful as vaccine or carrier for delivering a desired  
 antigen)

IT Gene, microbial

RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)

(phoP; microbes attenuated by inserting a transcription  
 terminator are useful as vaccine or carrier for delivering a desired  
 antigen)

IT Gene, microbial

RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)

(phoQ; microbes attenuated by inserting a transcription  
 terminator are useful as vaccine or carrier for delivering a desired  
 antigen)

IT Gene, microbial

RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)

(pmi; microbes attenuated by inserting a transcription  
 terminator are useful as vaccine or carrier for delivering a desired  
 antigen)

IT Gene, microbial

RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)

(pncB; microbes attenuated by inserting a transcription  
 terminator are useful as vaccine or carrier for delivering a desired  
 antigen)

- IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
 (poxR; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
 (pur; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
 (rfc; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
 (rpsL; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Gene, microbial  
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (rrfG 5S rRNA transcription terminator; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Operon  
 (rrnB, T1 or T2 transcription terminator; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Mutagenesis  
 (site-directed, deletion; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Mutagenesis  
 (site-directed, insertion; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Salmonella typhimurium  
 (strain MGN-1362, x8298 or x8429; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Genetic element  
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)  
 (terminator, transcription; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)
- IT Gene, microbial  
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (trpA, transcription terminator; microbes attenuated by inserting a transcription terminator are useful as vaccine or carrier for delivering a desired antigen)

IT 413009-57-1 413009-58-2 413009-59-3 413009-60-6 413009-61-7  
 413009-62-8 413009-63-9  
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
 (Biological study)  
 (nucleotide sequence; microbes attenuated by inserting a  
 transcription terminator are useful as vaccine or carrier for  
 delivering a desired antigen)

IT 413010-83-0 413010-84-1 413010-85-2 413010-86-3 413010-87-4  
 413010-88-5 413010-89-6 413010-90-9 413010-91-0 413010-92-1  
 413010-93-2 413010-94-3 413010-95-4 413010-96-5 413010-97-6  
 413010-98-7 413010-99-8  
 RL: PRP (Properties)  
 (unclaimed nucleotide sequence; microbes attenuated by  
 inserting a transcription terminator are useful as vaccine or carrier  
 for delivering a desired antigen)

IT 144095-73-8  
 RL: PRP (Properties)  
 (unclaimed sequence; microbes attenuated by inserting a  
 transcription terminator are useful as vaccine or carrier for  
 delivering a desired antigen)

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD  
 (1 CITINGS)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L128 ANSWER 8 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN DUPLICATE 8  
 ACCESSION NUMBER: 1999:343671 CAPLUS Full-text  
 DOCUMENT NUMBER: 130:351225  
 TITLE: Recombinant vaccines comprising immunogenic  
 attenuated bacteria having rpos positive  
 phenotype  
 INVENTOR(S): Curtiss, Roy, III; Nickerson, Cheryl A.  
 PATENT ASSIGNEE(S): Washington University, USA  
 SOURCE: PCT Int. Appl., 163 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9925387	A1	19990527	WO 1998-US24295	19981113
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6024961	A	20000215	US 1997-970789	19971114
CA 2309925	A1	19990527	CA 1998-2309925	19981113
CA 2309925	C	20100601		
AU 9914595	A	19990607	AU 1999-14595	19981113
AU 736242	B2	20010726		
EP 1030690	A1	20000830	EP 1998-958581	19981113
EP 1030690	B1	20020703		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				



JP 2001523649	T	20011127	JP 2000-520820	19981113
AT 219948	T	20020715	AT 1998-958581	19981113
ES 2181306	T3	20030216	ES 1998-958581	19981113
PRIORITY APPLN. INFO.:			US 1997-970789	A2 19971114
			WO 1998-US24295	W 19981113

# ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Attenuated immunogenic bacteria having an RpoS+ phenotype, in particular, Salmonella enterica serotype typhi having an RpoS+ phenotype and methods therefor are disclosed. The Salmonella have in addition to an RpoS+ phenotype an inactivating mutation in one or more genes which render the microbe attenuated, and a recombinant gene capable of expressing a desired protein. The Salmonella are attenuated and have high immunogenicity so that they can be used in vaccines and as delivery vehicles for genes and gene products. Also disclosed are methods for preparing the vaccine delivery vehicles. Described were vaccines containing the disclosed Salmonella delivery vehicle and hepatitis B nucleocapsid pre-S1 pre-S2 particles, interleukin 2, sperm-specific antigen ZP-3 (as contraceptive vaccine), NALT, BALT, CALT, GALT proteins, and others. IPCI A61K0048-00 [ICM,6]; C12N0001-22 [ICS,6]; A61K0039-112 [ICS,6]

IPCR C12N0015-09 [I,C\*]; C12N0015-09 [I,A]; A61K0035-66 [I,C\*]; A61K0035-74 [I,A]; A61K0038-17 [I,C\*]; A61K0038-17 [I,A]; A61K0038-19 [I,C\*]; A61K0038-19 [I,A]; A61K0039-112 [I,C\*]; A61K0039-112 [I,A]; A61K0039-12 [I,C\*]; A61K0039-12 [I,A]; A61K0039-29 [I,C\*]; A61K0039-29 [I,A]; A61K0039-35 [I,C\*]; A61K0039-35 [I,A]; A61K0048-00 [I,C\*]; A61K0048-00 [I,A]; A61P0031-00 [I,C\*]; A61P0031-00 [I,A]; A61P0031-04 [I,A]; C12N0001-21 [I,C\*]; C12N0001-21 [I,A]; C12N0001-22 [I,C\*]; C12N0001-22 [I,A]

CC 15-2 (Immunochemistry)

Section cross-reference(s): 3, 63

ST vaccine antigen delivery Salmonella RpoS gene; gene product delivery attenuated Salmonella RpoS

IT Sialoglycoproteins

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(ZP3 (zona pellucida, 3); recombinant vaccines comprising immunogenic attenuated bacteria having rpos pos. phenotype)

IT Gene, microbial

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(aro; recombinant vaccines comprising immunogenic attenuated bacteria having rpos pos. phenotype)

IT Gene, microbial

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(asd; recombinant vaccines comprising immunogenic attenuated bacteria having rpos pos. phenotype)

IT Antigens

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(autoantigens; recombinant vaccines comprising immunogenic attenuated bacteria having rpos pos. phenotype)

IT Drug delivery systems

(carriers; recombinant vaccines comprising immunogenic attenuated bacteria having rpos pos. phenotype)

IT Gene, microbial

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cdt; recombinant vaccines comprising immunogenic attenuated bacteria having rpos pos. phenotype)

IT Vaccines

(contraceptive; recombinant vaccines comprising immunogenic attenuated bacteria having rpos pos. phenotype)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (crp; recombinant vaccines comprising immunogenic attenuated bacteria having rpos pos. phenotype)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (cya; recombinant vaccines comprising immunogenic attenuated bacteria having rpos pos. phenotype)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (dap; recombinant vaccines comprising immunogenic attenuated bacteria having rpos pos. phenotype)

IT Proteins, general, biological studies  
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (foreign; recombinant vaccines comprising immunogenic attenuated bacteria having rpos pos. phenotype)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (fur; recombinant vaccines comprising immunogenic attenuated bacteria having rpos pos. phenotype)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (galE; recombinant vaccines comprising immunogenic attenuated bacteria having rpos pos. phenotype)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (galU; recombinant vaccines comprising immunogenic attenuated bacteria having rpos pos. phenotype)

IT Immunomodulators  
 Immunostimulants  
 Immunosuppressants  
 (gene product; recombinant vaccines comprising immunogenic attenuated bacteria having rpos pos. phenotype)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (hemA; recombinant vaccines comprising immunogenic attenuated bacteria having rpos pos. phenotype)

IT Antigens  
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (hepatitis B surface, pre-S1 protein; recombinant vaccines comprising immunogenic attenuated bacteria having rpos pos. phenotype)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (htrA; recombinant vaccines comprising immunogenic attenuated bacteria having rpos pos. phenotype)

IT Gene, microbial

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(nadA; recombinant vaccines comprising immunogenic attenuated  
bacteria having rpos pos. phenotype)

IT Virion structure  
(nucleocapsid, hepatitis B; recombinant vaccines comprising immunogenic  
attenuated bacteria having rpos pos. phenotype)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(ompR; recombinant vaccines comprising immunogenic attenuated  
bacteria having rpos pos. phenotype)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(pab; recombinant vaccines comprising immunogenic attenuated  
bacteria having rpos pos. phenotype)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(phoP; recombinant vaccines comprising immunogenic attenuated  
bacteria having rpos pos. phenotype)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(phoQ; recombinant vaccines comprising immunogenic attenuated  
bacteria having rpos pos. phenotype)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(pmi; recombinant vaccines comprising immunogenic attenuated  
bacteria having rpos pos. phenotype)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(pncB; recombinant vaccines comprising immunogenic attenuated  
bacteria having rpos pos. phenotype)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(poxR; recombinant vaccines comprising immunogenic attenuated  
bacteria having rpos pos. phenotype)

IT Gene  
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL  
(Biological study); PREP (Preparation); USES (Uses)  
(product; recombinant vaccines comprising immunogenic  
attenuated bacteria having rpos pos. phenotype)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(recombinant vaccines comprising immunogenic attenuated  
bacteria having RpoS pos. phenotype)

IT Bacteria (Eubacteria)  
Drug delivery systems  
Escherichia coli  
Fungi  
Gene therapy  
Hepatitis B virus  
Microorganism  
Mutation

Parasite

Pathogen

Protozoa

Salmonella

Salmonella choleraesuis

Salmonella dublin

Salmonella enterica

Salmonella enteritidis

Salmonella hirschfeldii

Salmonella paratyphi-A

Salmonella schottmuelleri

Salmonella typhi

Salmonella typhimurium

Shigella

Vaccines

Virus

(recombinant vaccines comprising immunogenic attenuated

bacteria having rpos pos. phenotype)

IT Gene, microbial

Interleukin 2

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)

(recombinant vaccines comprising immunogenic attenuated

bacteria having rpos pos. phenotype)

IT Allergens

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(recombinant vaccines comprising immunogenic attenuated

bacteria having rpos pos. phenotype)

IT Gene, microbial

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(rfc; recombinant vaccines comprising immunogenic attenuated

bacteria having rpos pos. phenotype)

IT Gene, microbial

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)

(rpoS; recombinant vaccines comprising immunogenic attenuated

bacteria having rpos pos. phenotype)

IT Gene, microbial

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(rpsL; recombinant vaccines comprising immunogenic attenuated

bacteria having rpos pos. phenotype)

IT Gamete and Germ cell

Sperm

(specific antigen; recombinant vaccines comprising immunogenic

attenuated bacteria having rpos pos. phenotype)

IT DNA

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)

(vaccine; recombinant vaccines comprising immunogenic

attenuated bacteria having rpos pos. phenotype)

IT Contraceptives

(vaccines; recombinant vaccines comprising immunogenic

attenuated bacteria having rpos pos. phenotype)

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD

(1 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L128 ANSWER 9 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN  
 ACCESSION NUMBER: 2010:499281 CAPLUS Full-text  
 DOCUMENT NUMBER: 152:499391  
 TITLE: Recombinant Salmonella typhi expressing Streptococcus  
 pneumoniae antigen as vaccine against Streptococcus  
 pneumoniae infection  
 INVENTOR(S): Curtiss, Roy., III; Santander-Morales,  
 Javier; Wanda, Soo-Young; Wang, Shifeng; Brenneman,  
 Karen; Shi, Huoying; Xin, Wei; Kong, Qingke  
 PATENT ASSIGNEE(S): Arizona State University, USA  
 SOURCE: PCT Int. Appl., 255pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2010045620	A1	20100422	WO 2009-US61100	20091016
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,			
	CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG,			
	ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP,			
	KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA,			
	MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE,			
	PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV,			
	SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,			
	IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI,			
	SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,			
	SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG,			
	ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: US 2008-106367P P 20081017  
 AB The invention encompasses a recombinant bacterium capable of eliciting an  
 immune response against Streptococcus pneumoniae, a vaccine comprising the  
 bacterium, and methods of using the bacterium. IPCI A61K0039-02 [I,A]  
 IPCR A61K0039-02 [I,C]; A61K0039-02 [I,A]  
 CC 15-2 (Immunochemistry)  
 Section cross-reference(s): 3, 10, 63  
 IT Cytolysis  
 (attenuated; recombinant Salmonella typhi expressing  
 Streptococcus pneumoniae antigen as vaccine against Streptococcus  
 pneumoniae infection)  
 IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (for; recombinant Salmonella typhi expressing Streptococcus  
 pneumoniae antigen as vaccine against Streptococcus pneumoniae  
 infection)  
 IT DNA sequences  
 Molecular cloning  
 Mutagenesis  
 Protein sequences  
 Salmonella typhi  
 Streptococcus pneumoniae  
 Vaccines

(recombinant *Salmonella typhi* expressing *Streptococcus pneumoniae* antigen as vaccine against *Streptococcus pneumoniae* infection)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L128 ANSWER 10 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:237843 CAPLUS Full-text

DOCUMENT NUMBER: 150:230569

TITLE: Bacterial expression hosts with regulated synthesis of antigens and regulated attenuation to increase the antigenicity of antigens and safety as live vaccines

INVENTOR(S): Curtiss, Roy, III; Wang, Shifeng; Wanda, Soo-Young; Kong, Wei

PATENT ASSIGNEE(S): Arizona State University, USA; Washington University

SOURCE: PCT Int. Appl., 191 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009025888	A2	20090226	WO 2008-US63293	20080509
WO 2009025888	A3	20090416		
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			
EP 2150616	A2	20100210	EP 2008-827622	20080509
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, AL, BA, MK, RS			
US 20100124558	A1	20100520	US 2009-615872	20091110
PRIORITY APPLN. INFO.:			US 2007-917313P	P 20070510
			WO 2008-US63293	W 20080509

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Methods of constructing bacterial strains for use as live vaccines with improved retention of the antigen genes and lowered antigenicity and virulence are described. These strains have the gene for the antigen under the control of a repressor encoded by a gene integrated into the bacterial chromosome. Virulence genes necessary to allow the vaccine strain to colonize lymphoid tissue are also placed under the control of a foreign promoter. This allows the expression of the gene to allow the bacterium to colonize lymphoid tissue. The gene is then repressed to prevent the progression to either a disease state or provocation of an immune response to the cell. The development of an arabinose-regulated system for use in *Salmonella enterica* serovar Typhimurium is demonstrated. *Escherichia coli* transcription factors and repressors were stable and functional in a *Salmonella* host. The bacteria are attenuated in mice and mice vaccinated with them resisted challenge with a virulent *S. enterica* serovar Typhimurium.

IPCI C12N0001-21 [I,A]; C12N0015-00 [I,C]; C12N0015-00 [I,A]

IPCR C12N0015-00 [I,C]; C12N0015-00 [I,A]

CC 3-2 (Biochemical Genetics)  
Section cross-reference(s): 15

ST live vaccine safety antigen attenuation regulated expression

IT Promoter (genetic element)  
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES  
(Uses)  
(PBAD, antigen gene expression from; bacterial expression hosts with regulated synthesis of antigens and regulated attenuation to increase antigenicity and safety as live vaccines)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(araC, arabinose-regulated promoter of; bacterial expression hosts with regulated synthesis of antigens and regulated attenuation to increase antigenicity and safety as live vaccines)

IT Promoter (genetic element)  
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES  
(Uses)  
(arabinose-regulated, lacI gene expression from; bacterial expression hosts with regulated synthesis of antigens and regulated attenuation to increase antigenicity and safety as live vaccines)

IT Transcription factors  
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES  
(Uses)  
(cI repressor, in regulated expression systems; bacterial expression hosts with regulated synthesis of antigens and regulated attenuation to increase antigenicity and safety as live vaccines)

IT Gene, microbial  
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES  
(Uses)  
(crp, regulated expression in attenuated vaccine strains; bacterial expression hosts with regulated synthesis of antigens and regulated attenuation to increase antigenicity and safety as live vaccines)

IT Gene, microbial  
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES  
(Uses)  
(fur, regulated expression in attenuated vaccine strains; bacterial expression hosts with regulated synthesis of antigens and regulated attenuation to increase antigenicity and safety as live vaccines)

IT Transcription factors  
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES  
(Uses)  
(gene cII, in regulated expression systems; bacterial expression hosts with regulated synthesis of antigens and regulated attenuation to increase antigenicity and safety as live vaccines)

IT Lymphatic system  
(gut-associated, vaccine strain colonization of; bacterial expression hosts with regulated synthesis of antigens and regulated attenuation to increase antigenicity and safety as live vaccines)

IT Gene, microbial  
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES  
(Uses)  
(lacI, in regulated expression systems; bacterial expression hosts with regulated synthesis of antigens and regulated attenuation to increase antigenicity and safety as live vaccines)

- IT Transcription factors  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES  
 (Uses)  
 (lactose repressors, in regulated expression systems; bacterial  
 expression hosts with regulated synthesis of antigens and regulated  
 attenuation to increase antigenicity and safety as live  
 vaccines)
- IT Salmonella paratyphi  
 Salmonella typhi  
 Streptococcus pneumoniae  
 (live vaccines against; bacterial expression hosts with regulated  
 synthesis of antigens and regulated attenuation to increase  
 antigenicity and safety as live vaccines)
- IT Immunity  
 (live vaccines for induction of; bacterial expression hosts with  
 regulated synthesis of antigens and regulated attenuation to  
 increase antigenicity and safety as live vaccines)
- IT Vaccines  
 (live; bacterial expression hosts with regulated synthesis of antigens  
 and regulated attenuation to increase antigenicity and safety  
 as live vaccines)
- IT Synthetic gene  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES  
 (Uses)  
 (microbial, lacI, in regulated expression systems; bacterial expression  
 hosts with regulated synthesis of antigens and regulated  
 attenuation to increase antigenicity and safety as live  
 vaccines)
- IT Gene, microbial  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES  
 (Uses)  
 (murA, regulated expression in attenuated vaccine strains;  
 bacterial expression hosts with regulated synthesis of antigens and  
 regulated attenuation to increase antigenicity and safety as  
 live vaccines)
- IT Gene, microbial  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES  
 (Uses)  
 (ompR, regulated expression in attenuated vaccine strains;  
 bacterial expression hosts with regulated synthesis of antigens and  
 regulated attenuation to increase antigenicity and safety as  
 live vaccines)
- IT Gene, microbial  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES  
 (Uses)  
 (phoPQ, regulated expression in attenuated vaccine strains;  
 bacterial expression hosts with regulated synthesis of antigens and  
 regulated attenuation to increase antigenicity and safety as  
 live vaccines)
- IT Gene, microbial  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES  
 (Uses)  
 (pspA, regulated expression in vaccine strains; bacterial expression  
 hosts with regulated synthesis of antigens and regulated  
 attenuation to increase antigenicity and safety as live  
 vaccines)
- IT Virulence (microbial)  
 (regulation in vaccine strains of; bacterial expression hosts with  
 regulated synthesis of antigens and regulated attenuation to  
 increase antigenicity and safety as live vaccines)



IT Genetic element  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES  
 (Uses)  
 (ribosome-binding site, in antigen expression cassette; bacterial  
 expression hosts with regulated synthesis of antigens and regulated  
 attenuation to increase antigenicity and safety as live  
 vaccines)

IT Gene, microbial  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES  
 (Uses)  
 (rpoS, regulated expression in attenuated vaccine strains;  
 bacterial expression hosts with regulated synthesis of antigens and  
 regulated attenuation to increase antigenicity and safety as  
 live vaccines)

IT Genetic element  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES  
 (Uses)  
 (signal sequence, in antigen expression cassette; bacterial expression  
 hosts with regulated synthesis of antigens and regulated  
 attenuation to increase antigenicity and safety as live  
 vaccines)

IT Gene, microbial  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES  
 (Uses)  
 (synthetic, lacI, in regulated expression systems; bacterial expression  
 hosts with regulated synthesis of antigens and regulated  
 attenuation to increase antigenicity and safety as live  
 vaccines)

IT Promoter (genetic element)  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES  
 (Uses)  
 (trc, antigen gene expression from; bacterial expression hosts with  
 regulated synthesis of antigens and regulated attenuation to  
 increase antigenicity and safety as live vaccines)

IT Salmonella  
 Salmonella enterica typhimurium  
 (vaccine host; bacterial expression hosts with regulated synthesis of  
 antigens and regulated attenuation to increase antigenicity  
 and safety as live vaccines)

IT Lymphatic system  
 (vaccine strain colonization of; bacterial expression hosts with  
 regulated synthesis of antigens and regulated attenuation to  
 increase antigenicity and safety as live vaccines)

IT 58-86-6, Xylose, biological studies 69-79-4, Maltose 147-81-9,  
 Arabinose 3615-41-6, Rhamnose  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES  
 (Uses)  
 (in regulation of antigen gene expression; bacterial expression hosts  
 with regulated synthesis of antigens and regulated attenuation  
 to increase antigenicity and safety as live vaccines)

IT 1116164-23-8 1116164-24-9 1116164-25-0 1116164-26-1 1116164-27-2  
 1116164-28-3 1116164-30-7 1116164-31-8 1116164-32-9 1116164-33-0  
 1116164-34-1 1116164-36-3 1116164-37-4 1116164-38-5 1116164-39-6  
 1116164-40-9 1116164-41-0 1116164-42-1 1116164-43-2 1116164-44-3  
 1116164-45-4 1116164-46-5 1116164-47-6 1116164-48-7 1116164-49-8  
 1116164-50-1 1116164-51-2 1116164-52-3 1116164-53-4 1116164-54-5  
 1116164-55-6 1116164-56-7 1116164-57-8 1116164-58-9 1116164-59-0  
 1116164-60-3 1116164-61-4 1116164-62-5 1116164-63-6 1116164-64-7  
 1116164-65-8 1116164-66-9 1116164-67-0 1116164-68-1 1116164-69-2  
 RL: PRP (Properties)

(unclaimed nucleotide sequence; bacterial expression hosts with regulated synthesis of antigens and regulated attenuation to increase the antigenicity of antigens and safety as live vaccines)

IT 1115861-88-5 1115861-89-6 1116164-29-4 1116164-35-2

RL: PRP (Properties)

(unclaimed protein sequence; bacterial expression hosts with regulated synthesis of antigens and regulated attenuation to increase the antigenicity of antigens and safety as live vaccines)

IT 1116164-70-5 1116164-71-6 1116164-72-7 1116164-73-8 1116164-74-9  
 1116164-75-0 1116164-76-1 1116164-77-2 1116164-78-3 1116164-79-4  
 1116164-80-7 1116164-81-8 1116164-82-9 1116164-83-0 1116164-84-1  
 1116164-85-2 1116164-86-3 1116164-87-4 1116164-88-5 1116164-89-6  
 1116164-90-9 1116164-91-0 1116164-92-1 1116164-93-2 1116164-94-3  
 1116164-95-4 1116164-96-5

RL: PRP (Properties)

(unclaimed sequence; bacterial expression hosts with regulated synthesis of antigens and regulated attenuation to increase the antigenicity of antigens and safety as live vaccines)

L128 ANSWER 11 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:203985 CAPLUS Full-text

DOCUMENT NUMBER: 140:248226

TITLE: Use of microorganisms that can be externally induced to lyse for the delivery of vaccine vectors and antigens to animal cells

INVENTOR(S): Curtiss, Roy, III; Kong, Wei

PATENT ASSIGNEE(S): Washington University, USA

SOURCE: PCT Int. Appl., 201 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004020643	A2	20040311	WO 2003-US26883	20030829
WO 2004020643	A3	20040408		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2003278729	A1	20040319	AU 2003-278729	20030829
EP 1537214	A2	20050608	EP 2003-770256	20030829
EP 1537214	B1	20060301		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
AT 318916	T	20060315	AT 2003-770256	20030829
US 20060140975	A1	20060629	US 2005-526365	20051115
PRIORITY APPLN. INFO.:			US 2002-407522P	P 20020901
			WO 2003-US26883	W 20030829

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Host/vector systems for delivery of antigens and eukaryotic expression constructs, especially vector vaccines, to animals using microorganisms is

described. The method uses a microorganism that is modified so that it can be induced to lyse by an external signal to release the antigen or vectors close to target cells. This allows use of hosts that will target a preferred cell type. Preferably, lysis is introduced by blocking expression of a gene essential for cell wall biosynthesis. The gene may be under control of a chemical regulated promoter that allows the host to grow normally in culture. When the cells are administered to a host, the expression of the essential gene stops and lysis occurs when the gene product has become too diluted by cell division to sustain cell wall biosynthesis. Development of strains of *Salmonella typhimurium* carrying the *asd* gene for semialdehyde dehydrogenase under control of an arabinose-regulated promoter is demonstrated. The cells were also modified to block the synthesis of cholanic acid and lipid A; to alter the expression of the *sifA* gene; to block the synthesis and utilization of D-alanine; block flagellum biosynthesis and to prevent premature termination of protein synthesis. These steps improve safety of the host cell. The cells were constructed using balanced-lethal suicide systems to avoid the use of antibiotic resistance markers. IPCI C12N0015-85 [ICM,7]; A61K0039-00 [ICS,7]

IPCR A61K0039-00 [I,C\*]; A61K0039-00 [I,A]; A61K0039-002 [I,C\*]; A61K0039-012 [I,A]; A61K0039-015 [I,A]; A61K0039-04 [I,C\*]; A61K0039-04 [I,A]; A61K0039-09 [I,C\*]; A61K0039-09 [I,A]; A61K0039-29 [I,C\*]; A61K0039-29 [I,A]; C12N0001-21 [I,C\*]; C12N0001-21 [I,A]; C12N0015-74 [I,C\*]; C12N0015-74 [I,A]

CC 3-2 (Biochemical Genetics)

Section cross-reference(s): 10, 15, 63

IT Promoter (genetic element)

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(aracPBAD, expression of essential genes from; use of microorganisms that can be externally induced to lyse for delivery of vaccine vectors and antigens to animal cells)

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L128 ANSWER 12 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2002:345842 CAPLUS Full-text

DOCUMENT NUMBER: 136:354186

TITLE: Recombinant vaccines comprising attenuated *Salmonella* having Rpos+ phenotype encoding a desired antigen

INVENTOR(S): Curtiss, Roy, III; Nickerson, Cheryl A.

PATENT ASSIGNEE(S): Washington University, USA

SOURCE: U.S., 50 pp., Cont.-in-part of U.S. 6,024,961.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
US 6383496	B1	20020507	US 1999-314062	19990518
US 6024961	A	20000215	US 1997-970789	19971114
ES 2181306	T3	20030216	ES 1998-958581	19981113
US 20030031683	A1	20030213	US 2002-138239	20020503
US 7083794	B2	20060801		

PRIORITY APPLN. INFO.: US 1997-970789 A2 19971114  
US 1999-314062 A1 19990518

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Attenuated immunogenic bacteria having an RpoS+ phenotype, in particular, *Salmonella enterica* serotype Typhi having an RpoS+ phenotype and methods therefor are disclosed. The *Salmonella* have in addition to an RpoS+ phenotype, an inactivating mutation in one or more genes which render the microbe attenuated, and a recombinant gene capable of expressing a desired protein. The inactivated/mutated genes are selected from *pab*, *pur*, *aro*, *asd*, *dap*, *nadA*, *pncB*, *balE*, *pmi*, *fur*, *rpsL*, *ompR*, *htrA*, *hemA*, *cdt*, *cya*, *crp*, *dam*, *phoP*, *phoQ*, *rfe*, *poxA*, *galU*, *metL*, *methH*, *mviA*, *sodC*, *recA*, *ssrA*, *ssrB*, *sirA*, *sirB*, *sirC*, *inv*, *hilA*, *hilC*, *hilD*, *rpoE*, *flgM*, *tonB* and *slyA* gene. The *Salmonella* are attenuated and have high immunogenicity so that they can be used in vaccines and as delivery vehicles for genes and gene products. Also disclosed are methods for preparing the vaccine delivery vehicles.

INCL 424200100

IPCI A61K0039-02 [ICM,7]; A61K0048-00 [ICS,7]; C12N0015-74 [ICS,7]; C12N0001-21 [ICS,7]

IPCR C12N0015-09 [I,C\*]; C12N0015-09 [I,A]; A61K0035-66 [I,C\*]; A61K0035-74 [I,A]; A61K0038-17 [I,C\*]; A61K0038-17 [I,A]; A61K0038-19 [I,C\*]; A61K0038-19 [I,A]; A61K0039-112 [I,C\*]; A61K0039-112 [I,A]; A61K0039-12 [I,C\*]; A61K0039-12 [I,A]; A61K0039-29 [I,C\*]; A61K0039-29 [I,A]; A61K0039-35 [I,C\*]; A61K0039-35 [I,A]; A61K0048-00 [I,C\*]; A61K0048-00 [I,A]; A61P0031-00 [I,C\*]; A61P0031-00 [I,A]; A61P0031-04 [I,A]; C12N0001-21 [I,C\*]; C12N0001-21 [I,A]; C12N0001-22 [I,C\*]; C12N0001-22 [I,A]

NCL 424/200.100; 424/093.200; 424/258.100; 435/252.300; 435/252.800; 435/471.000; 435/897.000

CC 15-2 (Immunochemistry)  
Section cross-reference(s): 2, 3, 10, 63

ST attenuated *Salmonella* Rpos pos phenotyp vaccine delivery

IT *Salmonella enterica*  
(*Choleraesuis* serotype; recombinant vaccines comprise attenuated *Salmonella* having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(Rpos; recombinant vaccines comprise attenuated *Salmonella* having Rpos+ phenotype expressing a desired antigen)

IT Eubacteria  
Phenotypes  
(Rpos+; recombinant vaccines comprise attenuated *Salmonella* having Rpos+ phenotype expressing a desired antigen)

IT Gamete and Germ cell  
(antigen; recombinant vaccines comprise attenuated *Salmonella* having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
(aro; recombinant vaccines comprise attenuated *Salmonella* having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
(asd; recombinant vaccines comprise attenuated *Salmonella* having Rpos+ phenotype expressing a desired antigen)

IT Antigens  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(autoantigens; recombinant vaccines comprise attenuated *Salmonella* having Rpos+ phenotype expressing a desired antigen)

- IT Organic compounds, biological studies  
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (biol., immunoregulatory; recombinant vaccines comprise attenuated Salmonella having Rpos+ phenotype expressing a desired antigen)
- IT Drug delivery systems  
 (carriers; recombinant vaccines comprise attenuated Salmonella having Rpos+ phenotype expressing a desired antigen)
- IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
 (cdt; recombinant vaccines comprise attenuated Salmonella having Rpos+ phenotype expressing a desired antigen)
- IT Drug delivery systems  
 (conjunctival; recombinant vaccines comprise attenuated Salmonella having Rpos+ phenotype expressing a desired antigen)
- IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
 (crp; recombinant vaccines comprise attenuated Salmonella having Rpos+ phenotype expressing a desired antigen)
- IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
 (cya; recombinant vaccines comprise attenuated Salmonella having Rpos+ phenotype expressing a desired antigen)
- IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
 (dam; recombinant vaccines comprise attenuated Salmonella having Rpos+ phenotype expressing a desired antigen)
- IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
 (dap; recombinant vaccines comprise attenuated Salmonella having Rpos+ phenotype expressing a desired antigen)
- IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
 (flgM; recombinant vaccines comprise attenuated Salmonella having Rpos+ phenotype expressing a desired antigen)
- IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
 (fur; recombinant vaccines comprise attenuated Salmonella having Rpos+ phenotype expressing a desired antigen)
- IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
 (galE; recombinant vaccines comprise attenuated Salmonella having Rpos+ phenotype expressing a desired antigen)
- IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)  
 (galU; recombinant vaccines comprise attenuated Salmonella having Rpos+ phenotype expressing a desired antigen)
- IT Antigens  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)  
 (gamete-specific; recombinant vaccines comprise attenuated  
 Salmonella having Rpos+ phenotype expressing a desired antigen)

IT Lymphatic system  
 (gut-associated, vaccine delivery; recombinant vaccines comprise  
 attenuated Salmonella having Rpos+ phenotype expressing a  
 desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (hemA; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (hila; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (hilC; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (hild; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (htrA; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (inv; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Bronchi  
 Nose  
 (lymphoid tissue vaccine delivery; recombinant vaccines comprise  
 attenuated Salmonella having Rpos+ phenotype expressing a  
 desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (meth; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (metL; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Immunomodulators  
 (mols.; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Drug delivery systems  
 (mucosal; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL

(Biological study); PROC (Process)  
 (mviA; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (nadA; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Drug delivery systems  
 (nasal; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (ompR; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Drug delivery systems  
 (oral; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);  
 THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)  
 (pab; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (phoP; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (phoQ; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (pmi; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (pncB; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (poxA; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (pur; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (recA; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

- IT Autoimmune disease
- Drug delivery systems
- Escherichia coli
- Eubacteria
- Fungi
- Genetic vectors
- Infection
- Molecular cloning
- Mutagenesis
- Parasite
- Pathogen
- Protozoa
  - Salmonella
  - Salmonella enterica dublin
  - Salmonella enterica enteritidis
  - Salmonella enterica typhimurium
  - Salmonella hirschfeldii
  - Salmonella paratyphi
  - Salmonella paratyphi-A
  - Salmonella schottmuelleri
  - Salmonella typhi
- Shigella
- Vaccines
- Virus
  - (recombinant vaccines comprise attenuated Salmonella having Rpos+ phenotype expressing a desired antigen)
- IT Allergens
- Antigens
- DNA
- Enzymes, biological studies
- Glycolipids
- Glycoproteins
- Hormones, animal, biological studies
- Lipoproteins
- Nucleic acids
- Peptides, biological studies
- Polynucleotides
- Polysaccharides, biological studies
- Proteins
- RNA
- RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
  - (recombinant vaccines comprise attenuated Salmonella having Rpos+ phenotype expressing a desired antigen)
- IT Drug delivery systems
  - (rectal; recombinant vaccines comprise attenuated Salmonella having Rpos+ phenotype expressing a desired antigen)
- IT Gene, microbial
  - RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
  - (rfe; recombinant vaccines comprise attenuated Salmonella having Rpos+ phenotype expressing a desired antigen)
- IT Gene, microbial
  - RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
  - (rpoE; recombinant vaccines comprise attenuated Salmonella having Rpos+ phenotype expressing a desired antigen)
- IT Transcription factors
  - RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL



(Biological study); USES (Uses)  
 (rpoS; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (rpsL; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (sirA; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (sirB; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (sirC; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (slyA; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (sodC; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (ssrA; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (ssrB; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL  
 (Biological study); PROC (Process)  
 (tonB; recombinant vaccines comprise attenuated Salmonella  
 having Rpos+ phenotype expressing a desired antigen)

IT Lymphatic system  
 (vaccine delivery; recombinant vaccines comprise attenuated  
 Salmonella having Rpos+ phenotype expressing a desired antigen)

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD  
 (6 CITINGS)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L128 ANSWER 13 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN  
 ACCESSION NUMBER: 2001:816942 CAPLUS Full-text  
 DOCUMENT NUMBER: 135:353768  
 TITLE: Regulated antigen delivery system (RADS) for live

bacterial vaccines  
 INVENTOR(S): Curtiss, Roy, III; Tinge, Steven A.  
 PATENT ASSIGNEE(S): Washington University, USA; Megan Health, Inc.  
 SOURCE: PCT Int. Appl., 95 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001083785	A2	20011108	WO 2001-US13915	20010430
WO 2001083785	A3	20020613		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 6780405	B1	20040824	US 2000-560539	20000428
CA 2407709	A1	20011108	CA 2001-2407709	20010430
EP 1292687	A2	20030319	EP 2001-944119	20010430
EP 1292687	B1	20060816		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
HU 2003000793	A2	20030728	HU 2003-793	20010430
NZ 522433	A	20040430	NZ 2001-522433	20010430
JP 2004515210	T	20040527	JP 2001-580392	20010430
BR 2001010408	A	20040622	BR 2001-10408	20010430
AT 336584	T	20060915	AT 2001-944119	20010430
ES 2271031	T3	20070416	ES 2001-944119	20010430
MX 2002010690	A	20040730	MX 2002-10690	20021028
IN 2002DN01086	A	20100305	IN 2002-DN1086	20021101
ZA 2002009267	A	20040212	ZA 2002-9267	20021114
US 20040137003	A1	20040715	US 2004-258931	20040112
US 20050106176	A1	20050519	US 2004-924574	20040824
US 7341860	B2	20080311		

PRIORITY APPLN. INFO.:  
 US 2000-560539 A1 20000428  
 WO 2001-US13915 W 20010430

# ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB We describe a regulated antigen delivery system (RADS) that has (a) a vector that includes (1) a gene encoding a desired gene product operably linked to a control sequence, (2) an origin of replication conferring vector replication using DNA polymerase III, and (3) an origin of replication conferring vector replication using DNA polymerase I, where the second origin of replication is operably linked to a control sequence that is repressible by a repressor. The RADS microorganism also has a gene encoding a repressor, operably linked to an activatable control sequence. The RADS described provide high levels of the desired gene product after repression of the high copy number origin of replication is lifted. The RADS are particularly useful as live bacterial vaccines. Also described is a delayed RADS system, in which there is a delay before the high copy number origin is expressed after the repression is lifted. The delayed RADS is also particularly useful for live bacterial vaccines. Also described are several control elements useful for these systems, as well as methods for providing immunity to a pathogen in a vertebrate immunized with the RADS microorganisms. The invention claims bacterial host strains, attenuated pathogenic bacteria such as Salmonella, which have

chromosomal deletions and insertions for maintenance of plasmid RAVs (runaway vectors). DNA constructs for the bacterial host strains are diagrammed. The invention further claims an RAV pMEG-771 for arabinose-regulated runaway expression and describes several derivs. PMEG-771 contains the pSC101 ori, the pUC ori downstream from the P22 PR promoter, genes repA and asd, and a multi-cloning site between the promoter Ptrc and the transcription terminator 5S T1T2. As examples of the invention, Erysipelothrix rhusiopathiae 65 kD surface antigen (Ery65) and Streptococcus equi M protein (SeM) were cloned in RAVs to produce pMEG-525 and pMEG-573 resp. Salmonella typhimurium and S. choleraesuis transformed with pMEG-525 showed an increase in plasmid copy number and Ery65 protein expression after transfer from culture medium with arabinose to medium without arabinose and after continued incubation without arabinose the bacteria become inviable. Mice immunized with the S. typhimurium recombinant strain containing pMEG-525 produced a strong antibody response to Ery65 antigen and were protected against a LD of E. rhusiopathiae. S. typhimurium pMEG-573 SeM vaccine strains produced a serum IgG SeM-specific immune response in mice and horses and also an IgA response in horses.

IPCI C12N0015-63 [ICM, 7]; C12N0015-74 [ICS, 7]; C12N0001-21 [ICS, 7]; A61K0039-00 [ICS, 7]; A61K0045-00 [ICS, 7]

IPCR C12N0015-09 [I,C\*]; C12N0015-09 [I,A]; A61K0039-00 [I,C\*]; A61K0039-00 [I,A]; A61K0039-112 [I,C\*]; A61K0039-112 [I,A]; A61P0037-00 [I,C\*]; A61P0037-04 [I,A]; C12N0001-21 [I,C\*]; C12N0001-21 [I,A]; C12N0015-63 [I,C\*]; C12N0015-63 [I,A]; C12N0015-74 [I,C\*]; C12N0015-74 [I,A]; C12P0021-02 [I,C\*]; C12P0021-02 [I,A]; C12R0001-42 [N,A]

CC 3-2 (Biochemical Genetics)  
Section cross-reference(s): 6, 10, 15, 63

IT Promoter (genetic element)  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(araCFEAD; regulated antigen delivery system (RADS) for live bacterial vaccines)

IT Gene targeting  
(gene knockin, araCFEAD-repressor gene; regulated antigen delivery system (RADS) for live bacterial vaccines)

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L128 ANSWER 14 OF 39 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1991:469825 CAPLUS Full-text

DOCUMENT NUMBER: 115:69825

ORIGINAL REFERENCE NO.: 115:12050h,12051a

TITLE: Cross-protective Salmonella vaccines using multiply mutant S. typhimurium

INVENTOR(S): Curtiss, Roy, III; Munson, Maryann

PATENT ASSIGNEE(S): Washington University, USA

SOURCE: PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9106317	A1	19910516	WO 1990-US6503	19901102
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2072633	A1	19910504	CA 1990-2072633	19901102

AU 9067371	A	19910531	AU 1990-67371	19901102
EP 500699	A1	19920902	EP 1990-917076	19901102
EP 500699	B1	19980610		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE				
JP 05504331	T	19930708	JP 1990-515888	19901102
AT 167061	T	19980615	AT 1990-917076	19901102
PRIORITY APPLN. INFO.:			US 1989-431597	A 19891103
			WO 1990-US6503	A 19901102

AB Attenuated Salmonella for use as live vaccines against Salmonella and other Gram-neg. bacteria are prepared. The organisms are incapable of manufacturing the lipopolysaccharide involved in pathogenesis because of mutation in several genes involved in the synthesis of, or regulation of synthesis of, the lipopolysaccharide. Other genes involved in the regulation of pathogenesis-related genes are also inactivated. A *S. typhimurium* with the *crp* and *cya* genes deleted was prepared by transposon mutagenesis with Tn10. *S. typhimurium* carrying both deletions had an LD50 of >10<sup>9</sup> colony-forming units (CFU) in Leghorn chicks, vs. 2 + 10<sup>4</sup> - 2 + 10<sup>5</sup> for wild-types. Similar deletions of the *phoP*, *fur*, *pmi*, and *galeE* genes were constructed. Some of the constructs prepared were found to confer cross-resistance to *S. enteritidis* and pathogenic *Escherichia coli*.

IPCI A61K0039-112 [ICM,5]

IPCR A61K0039-02 [I,C\*]; A61K0039-02 [I,A]; A61K0039-112 [I,C\*]; A61K0039-112 [I,A]; A61P0031-00 [I,C\*]; A61P0031-04 [I,A]; C12N0001-21 [I,C\*]; C12N0001-21 [I,A]; C12N0015-09 [I,C\*]; C12N0015-09 [I,A]; C12R0001-42 [N,A]

CC 15-2 (Immunochemistry)  
Section cross-reference(s): 10

IT Vaccines  
(Gram-neg. bacteria, cross-protective attenuated Salmonella for use in)

IT Salmonella  
*Salmonella typhimurium*  
(attenuated, for live cross-protective vaccine against Gram-neg. bacteria)

IT Receptors  
RL: PREP (Preparation)  
(for *cAMP*, gene for, of *Salmonella typhimurium*, deletion of, in preparation of live attenuated strains for vaccines cross-protective against Gram-neg. bacteria)

IT *Escherichia coli*  
*Salmonella enteritidis*  
(live vaccines against, attenuated *Salmonella typhimurium* for use in)

IT Lipopolysaccharides  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(*Salmonella* deficient in synthesis of, for use in live cross-protective vaccine against Gram-neg. bacteria)

IT Gene and Genetic element, microbial  
RL: PREP (Preparation)  
(*fur*, deletion from *Salmonella* genome of, for preparation of attenuated strains for live cross-protective vaccines against Gram-neg. bacteria)

IT Gene and Genetic element, microbial  
RL: PREP (Preparation)  
(*galeE*, deletion from *Salmonella* genome of, for preparation of attenuated strains for live cross-protective vaccines against Gram-neg. bacteria)

IT Gene and Genetic element, microbial  
RL: PREP (Preparation)  
(*phoP*, deletion from *Salmonella* genome of, for preparation of attenuated strains for live cross-protective vaccines against

Gram-neg. bacteria)

IT Gene and Genetic element, microbial  
 RL: PREP (Preparation)  
 (pmi, deletion from Salmonella genome of, for preparation of  
 attenuated strains for live cross-protective vaccines against  
 Gram-neg. bacteria)

IT Bacteria  
 (gram-neg., live vaccines against, attenuated Salmonella  
 typhimurium for use in)

IT Gene and Genetic element, microbial  
 RL: PREP (Preparation)  
 (crp, deletion from Salmonella genome of, for preparation of  
 attenuated strains for live cross-protective vaccines against  
 Gram-neg. bacteria)

IT Gene and Genetic element, microbial  
 RL: PREP (Preparation)  
 (cya, deletion from Salmonella genome of, for preparation of  
 attenuated strains for live cross-protective vaccines against  
 Gram-neg. bacteria)

IT 9012-42-4, Adenylate cyclase  
 RL: BIOL (Biological study)  
 (gene for, of Salmonella typhimurium, deletion of, in preparation of live  
 attenuated strains for vaccines cross-protective against  
 Gram-neg. bacteria)

IT 60-92-4  
 RL: BIOL (Biological study)  
 (receptor for, gene for, of Salmonella typhimurium, deletion of, in  
 preparation of live attenuated strains for vaccines  
 cross-protective against Gram-neg. bacteria)

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD  
 (4 CITINGS)

L128 ANSWER 15 OF 39 PASCAL COPYRIGHT 2010 INIST-CNRS. ALL RIGHTS RESERVED.  
 on STN

ACCESSION NUMBER: 2002-0329482 PASCAL Full-text

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 reserved.

TITLE (IN ENGLISH): Immune responses to recombinant pneumococcal PspA  
 antigen delivered by live attenuated

Salmonella enterica serovar Typhimurium vaccine

AUTHOR: HO YOUNG KANG; SRINIVASAN Jay; CURTISS Roy III

CORPORATE SOURCE: Department of Biology, Washington University, St.  
 Louis, Missouri 63130, United States

SOURCE: Infection and immunity, (2002), 70(4), 1739-1749, 59  
 refs.

ISSN: 0019-9567 CODEN: INFIBR

DOCUMENT TYPE: Journal

BIBLIOGRAPHIC LEVEL: Analytic

COUNTRY: United States

LANGUAGE: English

AVAILABILITY: INIST-15757, 354000100447180080

ABSTRACT: Attenuated Salmonella enterica serovar Typhimurium expressing  
 recombinant antigens from other pathogens elicits primarily a Th1-type dominant  
 immune response to both recombinant and Salmonella antigens. The immunogenicity and  
 appropriate subcellular location of the recombinant antigen in the Salmonella  
 vaccine strain may contribute to augmenting immune responses by facilitating  
 adequate exposure of recombinant antigen to antigen-presenting cells for

processing. To allow for secretion from gram-negative bacteria and overexpression of antigen, a DNA fragment encoding a highly antigenic  $\alpha$ -helical region of PspA (pneumococcal surface protein A) was subcloned downstream from the  $\beta$ -lactamase signal sequence in the multicopy Asd.sup.+ pYA3493 vector to create pYA3494. pYA3493 was derived from a class of Asd.sup.+ vectors with reduced expression of Asd to minimize selective disadvantage and enhance immunization of expressed recombinant antigens. The *S. enterica* serovar Typhimurium vaccine strain was constructed by the introduction of deletion mutations  $\Delta$ crp-28 and  $\Delta$ asdA16. Approximately 50% of the recombinant PspA (rPspA) expressed in a *Salmonella* strain harboring pYA3494 was detected in the combined supernatant and periplasmic fractions of broth-grown recombinant *Salmonella*. After a single oral immunization in BALB/c mice with 10<sup>9</sup> CFU of the recombinant *Salmonella* vaccine strain carrying pYA3494, immunoglobulin G (IgG) antibody responses were stimulated to both the heterologous antigen rPspA and *Salmonella* lipopolysaccharide (LPS) and outer membrane proteins (OMPs). About half, and even more at later times after immunization, of the antibodies induced to rPspA were IgG 1 (indicating a Th2-type response), whereas 60 to 70% of the antibodies to LPS and 80 to 90% of those to OMPs were IgG2a (indicating a Th1-type response). A sublethal infection with *Streptococcus pneumoniae* WU2 boosted PspA antibody levels and maintained IgG2a/IgG1 ratios similar to those seen before the challenge. Oral immunization with *Salmonella*-PspA vaccine protected 60% of immunized mice from death after intraperitoneal challenge with 50 times the 50% lethal dose of virulent *S. pneumoniae* WU2. CLASSIFICATION CODE: 002A05B12; Life sciences; Biological sciences;

Microbiology; Bacteriology; Immunology, Pharmacology  
002A05B10; Life sciences; Biological sciences;  
Microbiology; Bacteriology

## CONTROLLED TERM:

*Streptococcus pneumoniae*; *Salmonella*  
*typhimurium*; Mouse; *Streptococcus* A; Immune  
response; Antigen; Vaccine; Th1 lymphocyte;  
T-Lymphocyte; Immunogenicity; Vaccine strain;  
Accessory cell; *Salmonellosis*; *Streptococcal*  
infection; Antigenicity; Membrane protein; Secretion;  
Gram negative bacteria

## BROADER TERM:

*Streptococcaceae*; *Micrococcales*; Bacteria;  
*Enterobacteriaceae*; Rodentia; Mammalia; Vertebrata;  
Bacteriosis; Infection; Helper cell; Abnormal  
chromosome; Chromosomal aberration

L128 ANSWER 16 OF 39

WPIX COPYRIGHT 2010

THOMSON REUTERS on STN

DUPLICATE 5

ACCESSION NUMBER:

2004-042484 [200404] WPIX

DOC. NO. CPI:

C2004-017411 [200404]

TITLE:

New live attenuated derivative of a pathogenic  
*Enterobacteriaceae* species, useful as a vaccine for  
inducing cross protective immunity against infections  
caused by various *Enterobacteriaceae* strains or serotypes

DERWENT CLASS:

B04; C06; D16

INVENTOR:

CURTISS R

PATENT ASSIGNEE:

(UNIW-C) UNIV WASHINGTON; (UNIW-C) UNIV WASHINGTON OFFICE  
TECHNOLOGY MANAGE; (CURT-I) CURTISS R

COUNTRY COUNT:

102

## PATENT INFORMATION:

PATENT NO

KIND DATE

WEEK

LA PG

MAIN IPC

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WO 2003096812  A1 20031127 (200404)* EN 133[45]
AU 2003235457  A1 20031202 (200442) EN
EP 1499191     A1 20050126 (200508) EN
US 20060233829 A1 20061019 (200670) EN
AU 2003235457  B2 20090212 (200951) EN

```

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003096812	A1	WO 2003-US11802	20030415
US 20060233829	A1 Provisional	US 2002-372616P	20020415
US 20060233829	A1 Provisional	US 2002-373626P	20020418
AU 2003235457	A1	AU 2003-235457	20030415
EP 1499191	A1	EP 2003-721711	20030415
EP 1499191	A1	WO 2003-US11802	20030415
US 20060233829	A1	WO 2003-US11802	20030415
US 20060233829	A1	US 2005-511616	20051115
AU 2003235457	B2	AU 2003-235457	20030415

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003235457	A1 Based on	WO 2003096812 A
EP 1499191	A1 Based on	WO 2003096812 A
AU 2003235457	B2 Based on	WO 2003096812 A

PRIORITY APPLN. INFO: US 2002-373626P 20020418  
 US 2002-372616P 20020415  
 US 2005-511616 20051115  
 US 2002-372616P 20020415  
 US 2002-373626P 20020418

## INT. PATENT CLASSIF.:

IPC ORIGINAL: A61K0039-02 [I,A]; C12N0001-21 [I,A]; C12N0015-74 [I,A];  
 A61K0039-02 [I,C]; A61K0039-112 [I,A]; A61K0039-112 [I,C]  
 ; C12N0001-36 [I,A]; C12N0001-36 [I,C]

IPC RECLASSIF.: A61K0039-02 [I,A]; A61K0039-02 [I,C]; A61K0039-112 [I,A];  
 A61K0039-112 [I,C]; C12N0001-36 [I,A]; C12N0001-36 [I,C]

ECLA: A61K0039-02T1; A61K0039-02T3; C07K0014-255; C12N0001-36;  
 C12N0015-74

ICO: K61K0039:52B

USCLASS NCLM: 424/200.100

NCLS: 435/252.300; 435/471.000

## BASIC ABSTRACT:

WO 2003096812 A1 UPAB: 20090811

NOVELTY - A live attenuated derivative of a pathogenic Enterobacteriaceae species having enhanced ability to induce cross protective immunity against Enterobacteriaceae, is new.

DETAILED DESCRIPTION - A live attenuated derivative of a pathogenic Enterobacteriaceae species having enhanced ability to induce cross protective immunity against Enterobacteriaceae, comprising: (a) a means for regulatable expression of a gene encoding a regulatory protein, the expression of which in vivo causes synthesis of antigenic proteins that are conserved among Enterobacteriaceae; and (b) a means for regulatable synthesis of a second antigen, which ceases to be synthesized in vivo, exposing a carbohydrate antigen that is conserved among Enterobacteriaceae. INDEPENDENT CLAIMS are also included for: (1) a method for inducing a (cross-protective) immune

response sufficient for protection against infection by Enterobacteriaceae species, comprising administering live attenuated derivative defined above; (2) a vaccine comprising a live attenuated strain of Salmonella having enhanced ability to stimulate cross protective immunity against Enterobacteriaceae, consisting essentially of: (a) a mutation in a *pmi* gene that renders the *pmi* gene non functional; and (b) a genetic construction that allows for regulatable expression of a *fur* gene; and (3) a recombinant bacterial strain consisting essentially of a means of regulatable expression of a virulence gene, where the regulatable expression of a virulence gene renders the bacterial strain attenuated while maintaining immunogenicity. ACTIVITY - Antibacterial; Immunostimulant. Experimental protocols are described but no results are given. MECHANISM OF ACTION - Vaccine.

USE - The live attenuated derivatives are useful as vaccines for inducing high level immune response and/or cross protective immune response to protect individuals from infection from a diversity of species or serotypes of bacterial pathogens. TECHNOLOGY FOCUS:

BIOTECHNOLOGY - Preferred Derivative: The means of regulatable expression comprises substituting the promoter of the gene encoding a regulatory protein with a regulatable promoter. The regulatable promoter is the *araCP* BAD repressor-activator-promoter system. The carbohydrate antigen is an LPS O-antigen. The means for regulatable synthesis comprises a mutation in a gene that encodes a product necessary for synthesis of LPS O-antigen in the *pmi* gene. Specifically, the live attenuated derivative of a pathogenic Enterobacteriaceae species consists essentially of a means for regulatable expression of a *fur* gene, and a mutation that renders a *pmi* gene inoperable, where the means for regulatable expression of a ferric uptake regulator (*fur*) gene comprises substituting the *fur* promoter with a regulatable promoter or with *araCP*-BAD activator-repressor-promoter system. The means comprises the *DELTA**pmi*223::*araCP*-BAD genetic construction. The mutation that renders a *pmi* gene inoperable is preferably a deletion mutation. Alternatively, the attenuated derivative consists of a means for regulatable expression of a first surface antigen which is conserved among Enterobacteriaceae, and a means for regulatable expression of a second surface antigen, which is not conserved among Enterobacteriaceae, where up regulation of the first surface antigen and down regulation of the second surface antigen results in enhanced ability of the attenuated derivative to produce immunity against Enterobacteriaceae.

Preferred Method: Inducing an immune response to Enterobacteriaceae comprises administering to an individual a live attenuated derivative of a pathogenic Enterobacteriaceae capable of colonizing the intestinal tract, and reaching and persisting in the gut associated lymphoid tissue, where expression of at least one conserved surface antigen is up regulated and at least one non-conserved surface antigen is down regulated in the attenuated derivative when the attenuated derivative is in the lymphoid tissue of the individual.

#### EXTENSION ABSTRACT:

ADMINISTRATION - The derivatives may be administered orally, by gastric intubation, or as aerosols. No dosage given. EXAMPLE - A 1881-bp *Salmonella typhimurium* DNA sequence encompassing the *pmi* gene was PCR amplified from the *S. typhimurium* UK xi3761 chromosome. Specific oligonucleotides were designed to amplify the 298-bp sequence 5' to the ATG start codon of the *pmi* gene to



yield the N-flanking fragment, and the 301-bp sequence 3' to the TAG stop codon of the *pmi* gene to obtain the C-flanking fragment. The N- and C-flanking fragments were then digested with EcoRI, ligated, and digested to completion with KniI and SacI, and cloned into the suicide vector pMDS197, resulting to the vector pY3546. pYA3546 was introduced into the suicide vector donor strain MGN-617, which was then mated with *S. typhimurium* strain xi3761 and tetracycline-resistant transconjugants were selected. These transconjugants were grown in culture medium, and plated in the presence of 5% sucrose to select for a second crossover event to excise the suicide vector from the chromosome but leave in its place the deletion of 1176 bp encoding the *pmi* gene. One isolate designated xi8650 was stocked and the *pmi* allele designated *pmi*-2426.

FILE SEGMENT: CPI  
 MANUAL CODE: CPI: B04-B04C1; B04-E02; B04-E04; B04-E08; B04-F1000E;  
 B11-A01; B14-A01; B14-G01; B14-S11B; C04-B04C1; C04-E02;  
 C04-E04; C04-E08; C04-F0100E; C11-A01; C14-A01; C14-G01;  
 C14-S11B; D05-H04; D05-H07; D05-H08; D05-H12A; D05-H12D5;  
 D05-H12E; D05-H14A1; D05-H17A5; D05-H18

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 STN DUPLICATE 3

ACCESSION NUMBER: 2009:159133 BIOSIS Full-text  
 DOCUMENT NUMBER: PREV200900159133  
 TITLE: Regulated programmed lysis of recombinant Salmonella in  
 host tissues to release protective antigens and confer  
 biological containment.  
 AUTHOR(S): Kong, Wei; Wanda, Soo-Young; Zhang, Xin; Bollen, Wendy;  
 Tinge, Steven A.; Roland, Kenneth L.; Curtiss, Roy  
 [Reprint Author]  
 CORPORATE SOURCE: Arizona State Univ, Biodesign Inst, Ctr Infect Dis and  
 Vaccinol, Tempe, AZ 85287 USA  
 rcurtiss@asu.edu  
 SOURCE: Proceedings of the National Academy of Sciences of the  
 United States of America, (JUL 8 2008) Vol. 105, No. 27,  
 pp. 9361-9366.  
 CODEN: PNASA6. ISSN: 0027-8424.  
 DOCUMENT TYPE: Article  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: 25 Feb 2009  
 Last Updated on STN: 25 Feb 2009

ABSTRACT: We have devised and constructed a biological containment system designed to cause programmed bacterial cell lysis with no survivors. We have validated this system, using *Salmonella enterica*, serovar Typhimurium vaccines for antigen delivery after colonization of host lymphoid tissues. The system is composed of two parts. The first component is *Salmonella* \*\*\*typhimurium\*\*\* strain chi 8937, with deletions of *asdA* and arabinose-regulated expression of *murA*, two genes required for peptidoglycan synthesis and additional mutations to enhance complete lysis and antigen delivery. The second component is plasmid pYA3681, which encodes arabinose-regulated *murA* and *asdA* expression and C2-regulated synthesis of antisense *asdA* and *murA* mRNA transcribed from the P22 P-R promoter. An arabinose-regulated *c2* gene is present in the chromosome. chi 8937(pYA3681) exhibits arabinose-dependent growth. Upon invasion of host tissues, an arabinose-free environment, transcription of *asdA*, *murA*, and *c2* ceases, and concentrations of their gene products decrease because of cell division. The drop in C2 concentration results in activation of PR, driving synthesis of antisense mRNA to block translation of any residual *asdA* and *murA* mRNA. A

highly antigenic  $\alpha$ -helical domain of *Streptococcus pneumoniae* Rx1 PspA was cloned into pYA3681, resulting in pYA3685 to test antigen delivery. Mice orally immunized with chi 8937(pYA3685) developed antibody responses to PspA and *Salmonella* outer membrane proteins. No viable vaccine strain cells were detected in host tissues after 21 days. This system has potential applications with other Gram-negative bacteria in which biological containment would be desirable.

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CONCEPT CODE:      Genetics - Animal      03506
                     Physiology and biochemistry of bacteria      31000
                     Genetics of bacteria and viruses      31500
                     Immunology - General and methods      34502
INDEX TERMS:         Major Concepts
                     Infection; Immune System (Chemical Coordination and
                     Homeostasis)
INDEX TERMS:         Methods & Equipment
                     immunization: laboratory techniques, immunologic
                     techniques
ORGANISM:            Classifier
                     Enterobacteriaceae      06702
                     Super Taxa
                     Facultatively Anaerobic Gram-Negative Rods; Eubacteria;
                     Bacteria; Microorganisms
                     Organism Name
                     Salmonella typhimurium (species):
                     pathogen
                     Taxa Notes
                     Bacteria, Eubacteria, Microorganisms
ORGANISM:            Classifier
                     Gram-Positive Cocci      07700
                     Super Taxa
                     Eubacteria; Bacteria; Microorganisms
                     Organism Name
                     Streptococcus pneumoniae (species): pathogen
                     Taxa Notes
                     Bacteria, Eubacteria, Microorganisms
ORGANISM:            Classifier
                     Muridae      86375
                     Super Taxa
                     Rodentia; Mammalia; Vertebrata; Chordata; Animalia
                     Organism Name
                     mouse (common): host
                     Taxa Notes
                     Animals, Chordates, Mammals, Nonhuman Vertebrates,
                     Nonhuman Mammals, Rodents, Vertebrates
GENE NAME:           mouse murA gene (Muridae); mouse asdA gene (Muridae)

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STN DUPLICATE 9

ACCESSION NUMBER: 1999:469031 BIOSIS Full-text  
DOCUMENT NUMBER: PREV199900469031  
TITLE: Construction and evaluation of a DELTAcyA DELTAcrp  
Salmonella typhimurium strain expressing  
avian pathogenic Escherichia coli O78 LPS as a vaccine to  
prevent airsacculitis in chickens.  
AUTHOR(S): Roland, Kenneth [Reprint author]; Curtiss, Roy, III  
[Reprint author]; Sizemore, Donata [Reprint author]  
CORPORATE SOURCE: Megan Health, Inc., 3655 Vista Avenue, Saint Louis, MO,  
63110, USA  
SOURCE: Avian Diseases, (July-Sept., 1999) Vol. 43, No. 3, pp.  
429-441. print.

CODEN: AVDIAI. ISSN: 0005-2086.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 9 Nov 1999

Last Updated on STN: 9 Nov 1999

ABSTRACT: Avian pathogenic strains of *Escherichia coli* cause a number of extraintestinal diseases in poultry, including airsacculitis and colisepticemia. Expression of 078 lipopolysaccharide (LPS) is frequently associated with pathogenic isolates. *Salmonella*, a common poultry contaminant, is a major public health concern. The purpose of this work was to develop an *E. coli* vaccine for poultry with the use of an attenuated \*\*\**Salmonella*\*\*\* typhimurium carrier that would benefit both the bird and the consumer. Orally administered attenuated *S. typhimurium* DELTAcya DELTAcrp strains have been shown to provide excellent protection against wild-type *Salmonella* challenge in chickens. This work describes the construction of a DELTAcya DELTAcrp derivative of an avian pathogenic *S. typhimurium* that expresses both the homologous group B determinants (O1,4,5,12) and the heterologous *E. coli* 078 LPS O antigens. This was accomplished by inserting the *E. coli* rfb region, which encodes the genes required for 078 expression, into the chromosomal *cya* gene of *S. typhimurium*, creating a defined deletion/insertion mutation. A DELTAcrp \*\*\*mutation\*\*\* was introduced in a subsequent step. Expression of both \*\*\*O\*\*\* antigens was stable in vitro and in vivo. Vaccination of white leghorn chicks at day of hatch and 14 days with the recombinant vaccine strain induced serum immune responses against both *S. typhimurium* and *E. coli* LPS and protected the birds against subsequent challenge with an avian pathogenic *E. coli* 078 strain. Introduction of a mutation in *rfc*, which encodes the O antigen polymerase, reduced the chain length of the *S. typhimurium* LPS without affecting the expression of 078. The *rfc* mutation further enhanced the ability of the vaccine strain to protect chickens against *E. coli* challenge.

CONCEPT CODE: Poultry production - General and methods 27002  
 Pathology - General 12502  
 Bacteriology, general and systematic 30000  
 Immunology - General and methods 34502

INDEX TERMS: Major Concepts  
 Animal Husbandry (Agriculture); Immune System (Chemical Coordination and Homeostasis); Pathology

INDEX TERMS: Diseases  
 airsacculitis: bacterial disease

INDEX TERMS: Diseases  
 colisepticemia: bacterial disease

INDEX TERMS: Chemicals & Biochemicals  
*Escherichia coli* 078 lipopolysaccharide

ORGANISM: Classifier  
 Enterobacteriaceae 06702  
 Super Taxa  
 Facultatively Anaerobic Gram-Negative Rods; Eubacteria;  
 Bacteria; Microorganisms  
 Organism Name  
*Escherichia coli*  
*Salmonella typhimurium*: pathogen,  
 strain-delta-cya delta-crp

Taxa Notes  
 Bacteria, Eubacteria, Microorganisms

ORGANISM: Classifier  
 Galliformes 85536  
 Super Taxa  
 Aves; Vertebrata; Chordata; Animalia  
 Organism Name

chicken  
Taxa Notes  
Animals, Birds, Chordates, Nonhuman Vertebrates,  
Vertebrates

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STN DUPLICATE 10

ACCESSION NUMBER: 1999:250921 BIOSIS Full-text  
DOCUMENT NUMBER: PREV199900250921  
TITLE: Protection and immune responses induced by  
attenuated *Salmonella typhimurium*  
UK-1 strains.  
AUTHOR(S): Zhang, Xin; Kelly, Sandra M.; Bollen, Wendy; Curtiss,  
Roy, III [Reprint author]  
CORPORATE SOURCE: Department of Biology, Washington University, Saint Louis,  
MO, 63130, USA  
SOURCE: Microbial Pathogenesis, (March, 1999) Vol. 26, No. 3, pp.  
121-130. print.  
CODEN: MIPAEV. ISSN: 0882-4010.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 2 Jul 1999  
Last Updated on STN: 2 Jul 1999

ABSTRACT: We previously reported that *Salmonella typhimurium* SR-11 mutants with deletion mutations in the genes encoding adenylate cyclase (cya) and the cAMP receptor protein (crp) are avirulent and protective in mice. *Salmonella typhimurium* UK-1 is highly virulent for chicks (oral LD50 of  $3 \times 10^3$  CFU) and mice (oral LD50 of  $8.5 \times 10^3$  CFU) and is capable of lethal infections in pigs, calves and horses. We postulated that attenuated derivatives of this lethal strain would probably induce a higher level of protective immunity than achieved with \*\*\*attenuated\*\*\* derivatives of less virulent *S. typhimurium* strains such as SR11. To test this hypothesis, we have constructed *S. typhimurium* UK-1 DELTAcya-12 DELTAcrp-11 mutant strain chi3985 and its virulence plasmid cured derivative chi4095 to investigate their avirulence and immunogenicity in mice. We found that the mutants are avirulent and able to induce protective immune responses in BALB/c mice. These \*\*\*mutant\*\*\* strains retained wild-type ability to colonize the gut associated lymphoid tissue but reach and persist in spleen and liver at a significantly lower level than the wild-type parent strain. Mice survived oral infection with  $>1 \times 10^9$  CFU of chi3985 (the equivalent to 105 50% lethal doses of wild-type *S. typhimurium* UK-1) and were fully protected against challenge with 105 times the LD50 of the wild-type parent. Immunized mice developed a high level of serum IgG titre to *Salmonella* LPS and delayed-type hypersensitivity (DTH) response to *S. typhimurium* outer \*\*\*membrane\*\*\* proteins. Compared to the virulence plasmid-containing strain chi3985, the virulence plasmid cured DELTAcya DELTAcrp mutant strain chi4095 was more attenuated and less protective, as some mice immunized with chi4095 died when challenged with the wild-type UK-1 strain. This work demonstrates that *S. typhimurium* UK-1 DELTAcrp DELTAcya \*\*\*mutant\*\*\* strain may be a potential live vaccine to induce protective immunity against *Salmonella* infection or to deliver foreign antigens to the immune system.

CONCEPT CODE: Pharmacology - General 22002  
Biochemistry studies - General 10060  
Digestive system - General and methods 14001  
Genetics of bacteria and viruses 31500  
Medical and clinical microbiology - General and methods 36001  
Immunology - General and methods 34502

Bacteriology, general and systematic 30000  
 Blood - General and methods 15001

INDEX TERMS: Major Concepts  
 Immune System (Chemical Coordination and Homeostasis);  
 Infection; Molecular Genetics (Biochemistry and  
 Molecular Biophysics); Pharmacology

INDEX TERMS: Parts, Structures, & Systems of Organisms  
 gut associated lymphoid tissue: digestive system; liver:  
 digestive system; spleen: blood and lymphatics, immune  
 system

INDEX TERMS: Diseases  
 bacterial infection: bacterial disease  
 Bacterial Infections (MeSH)

INDEX TERMS: Chemicals & Biochemicals  
 attenuated *Salmonella* vaccine: vaccine;  
 outer membrane proteins; virulence  
 plasmid; IgG [immunoglobulin G]; LPS  
 [lipopolysaccharide]; *Salmonella*  
*typhimurium* crp gene [cAMP receptor protein  
 gene]: deletion mutation; *Salmonella*  
*typhimurium* cya gene [adenylate cyclase gene]:  
 deletion mutation

INDEX TERMS: Methods & Equipment  
 oral immunization: immunization method

INDEX TERMS: Miscellaneous Descriptors  
 bacterial challenge; bacterial colonization; bacterial  
 virulence; delayed-type hypersensitivity response;  
 immune responses; protective immunity: induction

ORGANISM: Classifier  
 Bovidae 85715  
 Super Taxa  
 Artiodactyla; Mammalia; Vertebrata; Chordata; Animalia  
 Organism Name  
 cow: animal model, calf  
 Taxa Notes  
 Animals, Artiodactyls, Chordates, Mammals, Nonhuman  
 Vertebrates, Nonhuman Mammals, Vertebrates

ORGANISM: Classifier  
 Enterobacteriaceae 06702  
 Super Taxa  
 Facultatively Anaerobic Gram-Negative Rods; Eubacteria;  
 Bacteria; Microorganisms  
 Organism Name  
*Salmonella typhimurium*: SR-11  
 mutants, attenuated UK-1 strains,  
 mutant strains, pathogen  
 Taxa Notes  
 Bacteria, Eubacteria, Microorganisms

ORGANISM: Classifier  
 Equidae 86145  
 Super Taxa  
 Perissodactyla; Mammalia; Vertebrata; Chordata; Animalia  
 Organism Name  
 horse: animal model  
 Taxa Notes  
 Animals, Chordates, Mammals, Nonhuman Vertebrates,  
 Nonhuman Mammals, Perissodactyls, Vertebrates

ORGANISM: Classifier  
 Galliformes 85536  
 Super Taxa

Aves; Vertebrata; Chordata; Animalia  
 Organism Name  
 chicken: animal model, chick  
 Taxa Notes  
 Animals, Birds, Chordates, Nonhuman Vertebrates,  
 Vertebrates  
 ORGANISM: Classifier  
 Muridae 86375  
 Super Taxa  
 Rodentia; Mammalia; Vertebrata; Chordata; Animalia  
 Organism Name  
 BALB/c mouse: animal model  
 Taxa Notes  
 Animals, Chordates, Mammals, Nonhuman Vertebrates,  
 Nonhuman Mammals, Rodents, Vertebrates  
 ORGANISM: Classifier  
 Suidae 85740  
 Super Taxa  
 Artiodactyla; Mammalia; Vertebrata; Chordata; Animalia  
 Organism Name  
 pig: animal model  
 Taxa Notes  
 Animals, Artiodactyls, Chordates, Mammals, Nonhuman  
 Vertebrates, Nonhuman Mammals, Vertebrates  
 REGISTRY NUMBER: 9012-42-4 (ADENYLATE CYCLASE)

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 STN  
 ACCESSION NUMBER: 2009:193250 BIOSIS Full-text  
 DOCUMENT NUMBER: PREV200900193250  
 TITLE: Improving DNA Vaccine Vector for Efficient Vaccine Delivery  
 Using Live Attenuated Bacterial Carrier.  
 AUTHOR(S): Kong, W. [Reprint Author]; Zhang, X.; Ashraf, S.;  
 Curtiss, R. III  
 CORPORATE SOURCE: Arizona State Univ, Phoenix, AZ USA  
 SOURCE: Abstracts of the General Meeting of the American Society  
 for Microbiology, (2008) Vol. 108, pp. 668.  
 Meeting Info.: 108th General Meeting of the  
 American-Society-for-Microbiology. Boston, MA, USA. June 01  
 -05, 2008. Amer Soc Microbiol.  
 ISSN: 1060-2011.  
 DOCUMENT TYPE: Conference; (Meeting)  
 Conference; (Meeting Poster)  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: 18 Mar 2009  
 Last Updated on STN: 18 Mar 2009  
 CONCEPT CODE: General biology - Symposia, transactions and proceedings  
 00520  
 Cytology - Human 02508  
 Genetics - General 03502  
 Genetics - Human 03508  
 Pathology - Therapy 12512  
 Pharmacology - General 22002  
 Pharmacology - Clinical pharmacology 22005  
 Pharmacology - Immunological processes and allergy 22018  
 Physiology and biochemistry of bacteria 31000  
 Genetics of bacteria and viruses 31500  
 Virology - General and methods 33502  
 Immunology - General and methods 34502  
 INDEX TERMS: Major Concepts

Pharmacology; Immune System (Chemical Coordination and Homeostasis); Molecular Genetics (Biochemistry and Molecular Biophysics)

INDEX TERMS: Parts, Structures, & Systems of Organisms  
cell wall

INDEX TERMS: Chemicals & Biochemicals  
enhanced green fluorescent protein [EGFP]; DNA vaccine: immunologic-drug, immunostimulant-drug, vaccine; DNA vector; bacterial plasmids; nuclease: degradation; pYA3650: DNA vaccine vector; araCPBAD  
activator-promoter complex; anti-sense mRNA: synthesis; SV40 promoter: DNA nuclear targeting sequence; BGH poly A; pYA4050: DNA vaccine vector; pYA4545

INDEX TERMS: Methods & Equipment  
live attenuated bacterial carrier: drug  
delivery device

INDEX TERMS: Miscellaneous Descriptors  
inflammatory response; vaccine delivery

ORGANISM: Classifier  
Enterobacteriaceae 06702  
Super Taxa  
Facultatively Anaerobic Gram-Negative Rods; Eubacteria; Bacteria; Microorganisms  
Organism Name  
Salmonella typhimurium (species)  
Taxa Notes  
Bacteria, Eubacteria, Microorganisms

ORGANISM: Classifier  
Hominidae 86215  
Super Taxa  
Primates; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
Int-407 cell line (cell\_line): host, human embryonic intestine cells  
Taxa Notes  
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGANISM: Classifier  
Orthomyxoviridae 03505  
Super Taxa  
Negative Sense ssRNA Viruses; Viruses; Microorganisms  
Organism Name  
Influenza virus (common)  
Taxa Notes  
Microorganisms, Negative Sense Single-Stranded RNA Viruses, Viruses

ORGANISM: Classifier  
Polyomaviridae 03117  
Super Taxa  
dsDNA Viruses; Viruses; Microorganisms  
Organism Name  
SV40 (common) [Simian virus 40 (species)]  
Taxa Notes  
Double-Stranded DNA Viruses, Microorganisms, Viruses

REGISTRY NUMBER: 180033-16-3 (enhanced green fluorescent protein)  
180033-16-3 (EGFP)  
9026-81-7 (nuclease)

GENE NAME: bacteria asdA gene (Bacteria): expression; bacteria murA gene (Bacteria): expression

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STN

ACCESSION NUMBER: 2008:193127 BIOSIS Full-text  
DOCUMENT NUMBER: PREV200800188968  
TITLE: Regulated programmed lysis of recombinant Salmonella in  
vivo to release protective antigens and confer biological  
containment.

AUTHOR(S): Kong, W. [Reprint Author]; Wanda, S-Y.; Zhang, X.; Bollen,  
W.; Tinge, S.; Curtiss, R. III  
CORPORATE SOURCE: Washington Univ, St Louis, MO 63130 USA  
SOURCE: Abstracts of the General Meeting of the American Society  
for Microbiology, (2007) Vol. 107, pp. 282-283.  
Meeting Info.: 107th General Meeting of the  
American-Society-for-Microbiology. Toronto, CANADA. 2007,.  
Amer Soc Microbiol.  
ISSN: 1060-2011.

DOCUMENT TYPE: Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English  
ENTRY DATE: Entered STN: 19 Mar 2008  
Last Updated on STN: 19 Mar 2008

CONCEPT CODE: General biology - Symposia, transactions and proceedings  
00520  
Genetics - General 03502  
Genetics - Animal 03506  
Biochemistry studies - Proteins, peptides and amino acids  
10064  
Biochemistry studies - Lipids 10066  
Biochemistry studies - Carbohydrates 10068  
Pathology - Therapy 12512  
Pharmacology - General 22002  
Pharmacology - Immunological processes and allergy 22018  
Physiology and biochemistry of bacteria 31000  
Genetics of bacteria and viruses 31500  
Immunology - General and methods 34502  
Medical and clinical microbiology - Bacteriology 36002

INDEX TERMS: Major Concepts  
Pharmacology; Infection; Immune System (Chemical  
Coordination and Homeostasis); Molecular Genetics  
(Biochemistry and Molecular Biophysics)

INDEX TERMS: Parts, Structures, & Systems of Organisms  
cell wall

INDEX TERMS: Diseases  
streptococcal infection: bacterial disease, prevention  
and control  
Streptococcal Infections (MeSH)

INDEX TERMS: Chemicals & Biochemicals  
lipopolysaccharide; diaminopimelic acid; arabinose;  
muramic acid; C2 protein; outer  
membrane protein; GDP-fucose; GDP-mannose;  
colanic acid; MurA: synthesis; Asd: synthesis;  
Salmonella typhimurium vaccine:  
immunologic-drug, immunostimulant-drug, oral  
administration

INDEX TERMS: Miscellaneous Descriptors  
cell lysis

ORGANISM: Classifier  
Gram-Positive Cocci 07700  
Super Taxa  
Eubacteria; Bacteria; Microorganisms



Organism Name  
     Streptococcus pneumoniae (species): pathogen  
 Taxa Notes  
     Bacteria, Eubacteria, Microorganisms  
 ORGANISM: Classifier  
     Muridae 86375  
 Super Taxa  
     Rodentia; Mammalia; Vertebrata; Chordata; Animalia  
 Organism Name  
     mouse (common): host, strain-BALB/c  
 Taxa Notes  
     Animals, Chordates, Mammals, Nonhuman Vertebrates,  
     Nonhuman Mammals, Rodents, Vertebrates  
 REGISTRY NUMBER: 583-93-7 (diaminopimelic acid)  
     147-81-9 (arabinose)  
     1114-41-6 (muramic acid)  
     15839-70-0 (GDP-fucose)  
     3123-67-9 (GDP-mannose)  
     9012-87-7 (colanic acid)  
 GENE NAME: Salmonella typhimurium relA gene  
     (Enterobacteriaceae): mutation;  
     Salmonella typhimurium murA gene  
     (Enterobacteriaceae); Salmonella  
     typhimurium asd gene (Enterobacteriaceae);  
     Salmonella typhimurium c2 gene  
     (Enterobacteriaceae); Salmonella  
     typhimurium gmd gene (Enterobacteriaceae): deletion  
     mutation; Salmonella typhimurium  
     fcl gene (Enterobacteriaceae): deletion mutation  
  
 L128 ANSWER 22 OF 39 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on  
 STN  
 ACCESSION NUMBER: 2008:193106 BIOSIS Full-text  
 DOCUMENT NUMBER: PREV200800188947  
 TITLE: Salmonella vaccine vectors displaying regulated delayed in  
     vivo attenuation to enhance immunogenicity.  
 AUTHOR(S): Curtiss, R. III [Reprint Author]; Wanda, S-Y.;  
     Zhang, X.; Gunn, B.  
 CORPORATE SOURCE: Arizona State Univ, Tempe, AZ 85287 USA  
 SOURCE: Abstracts of the General Meeting of the American Society  
     for Microbiology, (2007) Vol. 107, pp. 278.  
     Meeting Info.: 107th General Meeting of the  
     American-Society-for-Microbiology. Toronto, CANADA. 2007,.  
     Amer Soc Microbiol.  
     ISSN: 1060-2011.  
 DOCUMENT TYPE: Conference; (Meeting)  
     Conference; Abstract; (Meeting Abstract)  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: 19 Mar 2008  
     Last Updated on STN: 19 Mar 2008  
 CONCEPT CODE: General biology - Symposia, transactions and proceedings  
     00520  
     Genetics - General 03502  
     Biochemistry studies - Carbohydrates 10068  
     Enzymes - General and comparative studies: coenzymes  
     10802  
     Pathology - Therapy 12512  
     Blood - Blood and lymph studies 15002  
     Blood - Blood cell studies 15004  
     Pharmacology - General 22002

Pharmacology - Immunological processes and allergy 22018  
 Physiology and biochemistry of bacteria 31000  
 Genetics of bacteria and viruses 31500  
 Immunology - General and methods 34502

INDEX TERMS: Major Concepts  
                   Pharmacology; Immune System (Chemical Coordination and Homeostasis); Molecular Genetics (Biochemistry and Molecular Biophysics)

INDEX TERMS: Parts, Structures, & Systems of Organisms  
                   lymphoid tissues: blood and lymphatics

INDEX TERMS: Chemicals & Biochemicals  
                   mannose-6-phosphate; fructose-6-phosphate;  $\circ$   
                   antigen; phosphomannose isomerase [EC 5.3.1.8];  
                   Salmonella vaccine: immunologic-drug,  
                   immunostimulant-drug, oral administration, vaccine

INDEX TERMS: Miscellaneous Descriptors  
                   enhanced immunogenicity

ORGANISM: Classifier  
                   Enterobacteriaceae 06702  
                   Super Taxa  
                   Facultatively Anaerobic Gram-Negative Rods; Eubacteria;  
                   Bacteria; Microorganisms  
                   Organism Name  
                   Salmonella typhimurium (species)  
                   Taxa Notes  
                   Bacteria, Eubacteria, Microorganisms

REGISTRY NUMBER: 3672-15-9 (mannose-6-phosphate)  
                   643-13-0 (fructose-6-phosphate)  
                   9023-88-5 (phosphomannose isomerase)  
                   9023-88-5 (EC 5.3.1.8)

GENE NAME: Salmonella typhimurium rpoS gene  
                   (Enterobacteriaceae); Salmonella  
                   typhimurium fur gene  
                   (Enterobacteriaceae); Salmonella  
                   typhimurium phoPQ gene (Enterobacteriaceae);  
                   Salmonella typhimurium crp gene  
                   (Enterobacteriaceae)

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ACCESSION NUMBER: 2003:556367 BIOSIS Full-text  
 DOCUMENT NUMBER: PREV200300557028  
 TITLE: Construction and application of host-vector systems for DNA  
           vaccine vector delivery.

AUTHOR(S): Kong, W. [Reprint Author]; Wanda, S. Y. [Reprint Author];  
           Curtiss, R. III [Reprint Author]

CORPORATE SOURCE: Washington University, Saint Louis, MO, USA  
 SOURCE: Abstracts of the General Meeting of the American Society  
           for Microbiology, (2003) Vol. 103, pp. Z-016.  
           <http://www.asmsusa.org/mtgsrc/generalmeeting.htm>. cd-rom.  
           Meeting Info.: 103rd American Society for Microbiology  
           General Meeting. Washington, DC, USA. May 18-22, 2003.  
           American Society for Microbiology.  
           ISSN: 1060-2011 (ISSN print).

DOCUMENT TYPE: Conference; (Meeting)  
                   Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 26 Nov 2003  
                   Last Updated on STN: 26 Nov 2003

ABSTRACT: A novel bacterial host-vector system to deliver DNA vaccine vectors in

vivo was developed using attenuated *Salmonella typhimurium*. DNA vaccine vectors (pYA3650 and pYA3651) possess an eukaryotic DNA expression cassette flanked by transcription terminators, a regulatable araCP-\*\*\*BAD\*\*\* activator-promoter complex controlling the in vitro/in vivo expression of two genetically modified genes (asd and murA) necessary for synthesis of the rigid layer of the bacterial cell wall, a regulated synthesis of anti-sense mRNA to completely turn off in vivo translation of asdA and murA mRNA, and a replicon necessary for replication in bacteria but not in eukaryotic cells. The attenuated *S. typhimurium* possesses deletion and deletion-insertion mutations for the asdA, murA and araCBAD genes to regulate delayed lysis with bacteria colonizing lymphoid tissues and undergoing 5 to 10 generations of growth prior to lysis to release the DNA vaccine. The system is totally attenuated and exhibits complete biological containment with no survivors. *Eimeria acervulina* sporozoite and merozoite antigen genes with a Kozak translation initiation sequence and ATG start codon at the 5' terminus and an in-frame fusion of the FLAG sequence at the 3' terminus were cloned into the pYA3650 and pYA3651 vectors to evaluate the DNA vaccine host-vector delivery system.

CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520  
 Genetics - General 03502  
 Genetics - Animal 03506  
 Pathology - Therapy 12512  
 Pharmacology - General 22002  
 Pharmacology - Immunological processes and allergy 22018  
 Physiology and biochemistry of bacteria 31000  
 Genetics of bacteria and viruses 31500  
 Immunology - General and methods 34502  
 Food microbiology - General and miscellaneous 39008  
 Invertebrata: comparative, experimental morphology, physiology and pathology - Protozoa 64002

INDEX TERMS: Major Concepts  
 Bioprocess Engineering; Immune System (Chemical Coordination and Homeostasis); Infection; Methods and Techniques; Molecular Genetics (Biochemistry and Molecular Biophysics); Pharmacology

INDEX TERMS: Chemicals & Biochemicals  
 DNA vaccine: immunologic-drug, immunostimulant-drug; merozoite antigen genes; pYA3650: vaccine vector; pYA3651: vaccine vector; sporozoite antigen genes

INDEX TERMS: Methods & Equipment  
 bacterial host-vector vaccine delivery system: clinical techniques, immunologic techniques, laboratory techniques, therapeutic and prophylactic techniques; host-vector system construction: applied and field techniques

INDEX TERMS: Miscellaneous Descriptors  
 vaccine development

ORGANISM: Classifier  
 Enterobacteriaceae 06702  
 Super Taxa  
 Facultatively Anaerobic Gram-Negative Rods; Eubacteria; Bacteria; Microorganisms  
 Organism Name  
*Salmonella typhimurium* (species):  
 attenuated, vaccine candidate  
 Taxa Notes  
 Bacteria, Eubacteria, Microorganisms

ORGANISM: Classifier  
 Sporozoa 35400

Super Taxa  
 Protozoa; Invertebrata; Animalia  
 Organism Name  
 Eimeria acervulina (species): sporozoite  
 Taxa Notes

Animals, Invertebrates, Microorganisms, Protozoans  
 GENE NAME: Salmonella typhimurium araCBAD gene  
 (Enterobacteriaceae): deletion mutation,  
 deletion-insertion mutation; Salmonella  
 typhimurium asdA gene (Enterobacteriaceae):  
 deletion mutation, deletion-insertion  
 mutation; Salmonella typhimurium  
 murA gene (Enterobacteriaceae): deletion mutation  
 , deletion-insertion mutation

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ACCESSION NUMBER: 2002:609166 BIOSIS Full-text

DOCUMENT NUMBER: PREV200200609166

TITLE: Salmonella typhimurium UK-1  
 DELTAPfur::araC PBADfur DELTApmi  
 mutants are highly attenuated and induced  
 protective immunity in BALB/c Mice.

AUTHOR(S): Zhang, X. [Reprint author]; Kang, H. Y. [Reprint author];  
 Bollen, W. [Reprint author]; Curtiss, R., III  
 [Reprint author]

CORPORATE SOURCE: Washington University, Saint Louis, MO, USA

SOURCE: Abstracts of the General Meeting of the American Society  
 for Microbiology, (2002) Vol. 102, pp. 512-513. print.  
 Meeting Info.: 102nd General Meeting of the American  
 Society for Microbiology. Salt Lake City, UT, USA. May  
 19-23, 2002. American Society for Microbiology.  
 ISSN: 1060-2011.

DOCUMENT TYPE: Conference; (Meeting)  
 Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 27 Nov 2002

Last Updated on STN: 27 Nov 2002

ABSTRACT: Salmonella typhimurium UK-1 DELTAPfur::araC PBADfur DELTApmi mutants  
 were constructed and their  
 virulence and protective ability evaluated in BALB/c mice. 1) This study was  
 based on the facts that deletion of the fur gene of S.  
 typhimurium highly attenuated Salmonella but rendered it poorly  
 immunogenic, and that since LPS is needed for Salmonella to colonize the  
 intestinal tract and reach and persist in lymphoid organs necessary to  
 stimulate protective immunity, permanent rough mutants of Salmonella  
 have not been very effective when used as live oral vaccines. 2) Defined  
 \*\*\*DELTApmi\*\*\* -2426 and DELTAPfur::araC PBADfur mutants  
 were constructed and evaluated in mice. These mutants enable  
 regulatable synthesis of LPS and expression of fur, respectively. We found  
 that although strains with either mutation protected mice against  
 challenge with the wild-type parent at 104-fold the LD50, each exhibited  
 virulence as indicated by some death in groups of mice receiving high doses. 3)  
 Strains with both the DELTApmi-2426 and DELTAPfur::araC  
 PBADfur deletion mutations exhibited high attenuation and  
 immunogenicity. Mice survived inoculation with >10<sup>9</sup> CFU of the  
 \*\*\*DELTApmi\*\*\* DELTAPfur::araC PBADfur mutant strain and  
 were protected against challenge with the wild-type parent at 105 times the  
 LD50. Furthermore, cross protective immunity against other Salmonella  
 serotypes was also observed. These results indicate that the DELTAPfur

:::araC PBADfur DELTApmi mutant may serve as an improved vaccine candidate against a diversity of Salmonella subspecies I serotypes.

CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520  
 Genetics - General 03502  
 Genetics - Animal 03506  
 Biochemistry studies - Lipids 10066  
 Biochemistry studies - Carbohydrates 10068  
 Physiology and biochemistry of bacteria 31000  
 Genetics of bacteria and viruses 31500  
 Immunology - General and methods 34502

INDEX TERMS: Major Concepts  
 Immune System (Chemical Coordination and Homeostasis);  
 Infection; Molecular Genetics (Biochemistry and Molecular Biophysics)

INDEX TERMS: Chemicals & Biochemicals  
 LPS [lipopolysaccharide]; live oral vaccine

INDEX TERMS: Miscellaneous Descriptors  
 deletion mutations; Meeting Abstract

ORGANISM: Classifier  
 Enterobacteriaceae 06702  
 Super Taxa  
 Facultatively Anaerobic Gram-Negative Rods; Eubacteria;  
 Bacteria; Microorganisms  
 Organism Name  
 Salmonella typhimurium: pathogen  
 Taxa Notes  
 Bacteria, Eubacteria, Microorganisms

ORGANISM: Classifier  
 Muridae 86375  
 Super Taxa  
 Rodentia; Mammalia; Vertebrata; Chordata; Animalia  
 Organism Name  
 BALB/c mouse  
 Taxa Notes  
 Animals, Chordates, Mammals, Nonhuman Vertebrates,  
 Nonhuman Mammals, Rodents, Vertebrates

GENE NAME: Salmonella typhimurium fur  
 gene (Enterobacteriaceae)

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ACCESSION NUMBER: 2002:223181 BIOSIS Full-text  
 DOCUMENT NUMBER: PREV200200223181  
 TITLE: Induction of Th 2-type immune responses against recombinant  
 PspA antigen delivered by attenuated live  
 Salmonella typhimurium vaccines.

AUTHOR(S): Kang, H. Y. [Reprint author]; Curtiss, R., III  
 [Reprint author]

CORPORATE SOURCE: Washington University, Saint Louis, MO, USA  
 SOURCE: Abstracts of the General Meeting of the American Society  
 for Microbiology, (2001) Vol. 101, pp. 336. print.  
 Meeting Info.: 101st General Meeting of the American  
 Society for Microbiology. Orlando, FL, USA. May 20-24,  
 2001. American Society of Microbiology.  
 ISSN: 1060-2011.

DOCUMENT TYPE: Conference; (Meeting)  
 Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 3 Apr 2002

Last Updated on STN: 3 Apr 2002

**ABSTRACT:** Attenuated *Salmonella typhimurium* expressing foreign antigens primarily elicit a Th 1 dominant immune response to both foreign and *Salmonella* antigens. We hypothesized that a proper antigen modification including subcellular location of foreign antigen and/or changing *Salmonella* surface adhesins might result in a different interaction with antigen presenting cells, and induce augmented levels of a Th 2-type immune response. Various mutations for expression of aggregative thin fimbriae (Agf) were constructed and introduced into an attenuated *S. typhimurium* DELTAcrp strain. A DELTAasd mutation was also introduced into the attenuated *Salmonella* strains to establish a balanced-lethal vector-host system allowing stable maintenance of the Asd+ expression vector. The highly antigenic alpha-helical region of PspA (pneumococcal surface protein A) was subcloned as a fusion to the beta-lactamase signal sequence on a multicopy Asd+ periplasmic secretion vector. The majority of the recombinant PspA expressed in *Salmonella* was detected in the supernatant and periplasmic fractions. After single oral immunization of BALB/c mice with 10<sup>9</sup> CFU, the recombinant *Salmonella*-PspA vaccine strains stimulated IgG antibody responses to both the heterologous antigen PspA and *Salmonella* outer \*\*\*membrane\*\*\* proteins (SOMPs). Regardless of the *Salmonella* carrier strain genotype, the induced antibody response was higher to PspA than to SOMPs with a higher anti-PspA titer of IgG1 than IgG2a. A sublethal challenge with *Streptococcus pneumoniae* WU2 boosted PspA antibody levels and maintained similar IgG2a/IgG1 ratios as seen before the challenge. All *Salmonella* vaccines, except a strain carrying a deletion of the agfBAC operon, induced a predominant (80 to 90%) IgG2a isotype response to SOMPs.

**CONCEPT CODE:** General biology - Symposia, transactions and proceedings  
00520  
Cytology - Animal 02506  
Physiology and biochemistry of bacteria 31000  
Immunology - General and methods 34502

**INDEX TERMS:** Major Concepts  
Immune System (Chemical Coordination and Homeostasis);  
Infection

**INDEX TERMS:** Parts, Structures, & Systems of Organisms  
T helper cell type 2: immune system

**INDEX TERMS:** Chemicals & Biochemicals  
attenuated live bacterial vaccine: vaccine;  
immunoglobulin G1; immunoglobulin G2a; outer  
membrane protein; pneumococcal surface protein A  
[PspA]

**INDEX TERMS:** Miscellaneous Descriptors  
immune response; immunization; Meeting Abstract

**ORGANISM:** Classifier  
Enterobacteriaceae 06702  
Super Taxa  
Facultatively Anaerobic Gram-Negative Rods; Eubacteria;  
Bacteria; Microorganisms  
Organism Name  
*Salmonella typhimurium*: pathogen  
Taxa Notes  
Bacteria, Eubacteria, Microorganisms

**ORGANISM:** Classifier  
Gram-Positive Cocci 07700  
Super Taxa  
Eubacteria; Bacteria; Microorganisms  
Organism Name  
*Streptococcus pneumoniae*: pathogen  
Taxa Notes  
Bacteria, Eubacteria, Microorganisms

ORGANISM: Classifier  
Muridae 86375  
Super Taxa  
Rodentia; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
mouse: animal model  
Taxa Notes  
Animals, Chordates, Mammals, Nonhuman Vertebrates,  
Nonhuman Mammals, Rodents, Vertebrates

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ACCESSION NUMBER: 1995:290786 BIOSIS Full-text  
DOCUMENT NUMBER: PREV199598305086  
TITLE: Involvement of cyclic AMP in the expression of iron induced  
adhesiveness in Salmonella.  
AUTHOR(S): Amin, Iqbal I.; Burns-Keliher, Lisa; Curtiss, Roy,  
III  
CORPORATE SOURCE: Washington Univ., St. Louis, MO 63130, USA  
SOURCE: Abstracts of the General Meeting of the American Society  
for Microbiology, (1995) Vol. 95, No. 0, pp. 257.  
Meeting Info.: 95th General Meeting of the American Society  
for Microbiology. Washington, D.C., USA. May 21-25, 1995.  
ISSN: 1060-2011.

DOCUMENT TYPE: Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 5 Jul 1995  
Last Updated on STN: 5 Jul 1995

CONCEPT CODE: General biology - Symposia, transactions and proceedings  
00520  
Cytology - Animal 02506  
Cytology - Human 02508  
Biochemistry studies - Nucleic acids, purines and  
pyrimidines 10062  
Biochemistry studies - Proteins, peptides and amino acids  
10064  
Biochemistry studies - Minerals 10069  
Biophysics - Molecular properties and macromolecules  
10506  
Biophysics - Membrane phenomena 10508  
Metabolism - Minerals 13010  
Metabolism - Proteins, peptides and amino acids 13012  
Metabolism - Nucleic acids, purines and pyrimidines 13014  
Physiology and biochemistry of bacteria 31000  
Genetics of bacteria and viruses 31500

INDEX TERMS: Major Concepts  
Biochemistry and Molecular Biophysics; Cell Biology;  
Genetics; Membranes (Cell Biology); Metabolism;  
Physiology

INDEX TERMS: Chemicals & Biochemicals  
CYCLIC AMP; IRON; ADENYLATE CYCLASE

INDEX TERMS: Miscellaneous Descriptors  
ADENYLATE CYCLASE; CYCLIC AMP RECEPTOR PROTEIN;  
FERRIC UPTAKE REGULATOR;  
INVA; INVB; INVC; INVD; INVH; IRON INDUCED ADHESIN GENE;  
MEETING ABSTRACT; MUTATION; STRAIN TML

ORGANISM: Classifier  
Enterobacteriaceae 06702  
Super Taxa

Facultatively Anaerobic Gram-Negative Rods; Eubacteria;  
Bacteria; Microorganisms

Organism Name

*Salmonella typhimurium*

Taxa Notes

Bacteria, Eubacteria, Microorganisms

ORGANISM:

Classifier

Galliformes 85536

Super Taxa

Aves; Vertebrata; Chordata; Animalia

Organism Name

chicken

Taxa Notes

Animals, Birds, Chordates, Nonhuman Vertebrates,  
Vertebrates

ORGANISM:

Classifier

Hominidae 86215

Super Taxa

Primates; Mammalia; Vertebrata; Chordata; Animalia

Organism Name

Hominidae

Taxa Notes

Animals, Chordates, Humans, Mammals, Primates,  
Vertebrates

REGISTRY NUMBER:

60-92-4 (CYCLIC AMP)

7439-89-6 (IRON)

9012-42-4 (ADENYLATE CYCLASE)

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ACCESSION NUMBER: 1994:330544 BIOSIS Full-text

DOCUMENT NUMBER: PREV199497343544

TITLE: Characterization of a deletion mutant of  
*Salmonella typhimurium* UK-1 affecting  
colonization of deep tissue.

AUTHOR(S): Bollen, W. S.; Burns-Keliher, L.; Tinge, S. A.; Zhang, X.;  
Curtiss, R., III

CORPORATE SOURCE: Washington Univ., St. Louis, MO, USA

SOURCE: Abstracts of the General Meeting of the American Society  
for Microbiology, (1994) Vol. 94, No. 0, pp. 85.  
Meeting Info.: 94th General Meeting of the American Society  
for Microbiology. Las Vegas, Nevada, USA. May 23-27, 1994.  
ISSN: 1060-2011.

DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 2 Aug 1994

Last Updated on STN: 2 Aug 1994

CONCEPT CODE: General biology - Symposia, transactions and proceedings  
00520

Biochemistry studies - Proteins, peptides and amino acids  
10064

Biophysics - Membrane phenomena 10508

Digestive system - Pathology 14006

Blood - Lymphatic tissue and reticuloendothelial system  
15008

Genetics of bacteria and viruses 31500

Medical and clinical microbiology - Bacteriology 36002

INDEX TERMS: Major Concepts

Blood and Lymphatics (Transport and Circulation);



INDEX TERMS: Digestive System (Ingestion and Assimilation); Genetics;  
Infection; Membranes (Cell Biology)  
Miscellaneous Descriptors  
CRP GENE; LIVER; MEETING ABSTRACT; OUTER  
MEMBRANE PROTEINS; SPLEEN; VIRULENCE

ORGANISM: Classifier  
Enterobacteriaceae 06702  
Super Taxa  
Facultatively Anaerobic Gram-Negative Rods; Eubacteria;  
Bacteria; Microorganisms  
Organism Name  
Enterobacteriaceae  
Taxa Notes  
Bacteria, Eubacteria, Microorganisms

ORGANISM: Classifier  
Muridae 86375  
Super Taxa  
Rodentia; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
mouse  
Taxa Notes  
Animals, Chordates, Mammals, Nonhuman Vertebrates,  
Nonhuman Mammals, Rodents, Vertebrates

L128 ANSWER 28 OF 39 BIOTECHDS COPYRIGHT 2010 THOMSON REUTERS on STN

ACCESSION NUMBER: 2003-18332 BIOTECHDS Full-text

TITLE: Novel carrier microbe for delivering desired gene product to  
a human, comprises a live attenuated bacteria  
having a recombinant rpoS+ gene, inactivating  
mutations, and a recombinant gene encoding desired  
gene product;  
recombinant vaccine preparation for use in infection  
therapy

AUTHOR: CURTISS R; NICKERSON C A

PATENT ASSIGNEE: CURTISS R; NICKERSON C A

PATENT INFO: US 20030031683 13 Feb 2003

APPLICATION INFO: US 2002-138239 3 May 2002

PRIORITY INFO: US 2002-138239 3 May 2002; US 1997-970789 14 Nov 1997

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2003-466217 [44]

ABSTRACT: DERWENT ABSTRACT:

NOVELTY - A carrier microbe (I) for the delivery of a desired gene product to a human, comprising a live attenuated bacteria having a recombinant rpoS+ gene, one or more inactivating mutations which render the microbe attenuated, and a second recombinant gene encoding the desired gene product, is new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) producing (M1) a strain of (I), by selecting a strain of bacteria having an RpoS+ phenotype by performing a test to determine the RpoS phenotype of the strain, producing one or more inactivating mutations which render the strain attenuated, and introducing into the strain a recombinant gene encoding a desired gene product; (2) producing carrier microbes for delivery of a desired gene product to a human, by generating a strain of the above mentioned live attenuated bacteria; (3) a composition (II) for immunizing a human, comprising the above mentioned live attenuated strain of bacteria; (4) a genetically engineered cell (III) comprising the above mentioned live attenuated strain of bacteria; and (5)

assessing (M2) immunogenicity of a bacteria, by determining the RpoS phenotype of the bacteria, where the presence of RpoS+ phenotype indicates increased immunogenicity compared to an isogenic bacteria having RpoS- phenotype. BIOTECHNOLOGY - Preferred Carrier Microbe: (I) is Salmonella, preferably S.typhi. The attenuated S.typhi comprises an inactivating mutation in a gene such as pab, pur, aro, asd, dap, nadA, pncB, galE, pmi, fur, rpsL, ompR, htrA, hemA, cdt, cya, crp, dam, phoP, phoQ, rfc, poxA, galU, metL, meth, mviA, sodC, recA, ssrA, ssrB, sirA, sirB, sirC, inv, hila, hilC, hild, rpoE, flgM, tonB, slyA and their combinations. The second recombinant gene encodes a product from a pathogen (such as virus, bacterium, protozoan, parasite or fungus) to the human, and encodes a product capable of suppressing, modulating, or augmenting an immune response in the human. The second recombinant gene encodes an auto-antigen, such as gamete-specific antigen, or encodes an allergen to the human, a cytokine that suppresses tumor growth and spread, an enzyme that converts a non-toxic prodrug into an anti-tumor drug or tumor-specific antigen. Preferred Composition: The attenuated strain is in a carrier. Preferred Engineered Cell: (III) comprises the live attenuated bacteria having a recombinant virulence gene is capable of expressing a gene product that facilitate invasion and colonization of the gut associated lymphoid tissues. Preferred Method: In M2, the RpoS phenotype is determined by assessing one or both catalase activity and glycogen biosynthesis activity of S.typhi. ACTIVITY - Antibacterial; Virucide; Fungicide; Protozoacide. MECHANISM OF ACTION - Vaccine. Superior immunogenicity of an attenuated RpoS+ strain of S.typhimurium following intranasal administration compared to the immunogenicity of the corresponding RpoS- strain administered by the same route was demonstrated. For each attenuated bacterial vaccine strain, intranasal immunizations were performed with eight-week-old female BALB/c mice such that each mouse received either 10<sup>9</sup> or 10<sup>8</sup> colony forming unit (cfu). Immunization was accomplished by inoculating each nostril with 0.005 ml (5 microl) of suspension or one nostril with 0.01 ml (10 microl) of suspension, or in the case of the controls with BSG lacking any bacteria. Food and water were returned within 30 minutes following intranasal immunization. Intranasally immunized mice and non-immunized controls were orally challenged with either 10<sup>8</sup> or 10<sup>9</sup> cfu of the wild-type virulent S.typhimurium strain, X3339, 30 days after the date of intranasal immunization. The X3339 challenge strain was grown overnight. The following morning the culture was diluted 1:200 into L broth and aerated at 37 degrees C until reaching an OD<sub>600</sub> of 0.8. The cells were concentrated by centrifugation followed by suspension in BSG. The mice to be perorally challenged were deprived of food and water for approximately 4 hours prior to the oral challenge. Mice were observed over a period of 30 days for morbidity and mortality. Intranasal administration of both the RpoS+ microbe (X8296) and the RpoS- microbe (X8308) provided some protection against challenge by the wild-type strain (X3339). The RpoS+ strain was more effective, however, in this strain provided greater protection against challenge with the wild-type strain (5 out of 16 survivors) than did the corresponding RpoS- strain (2 out of 16 survivors).

USE - (I) is useful for delivery of a desired gene product to a human by selecting for a live attenuated strain of bacteria,

and administering the strain to the human, or directly administering the live attenuated bacteria to the human. The recombinant virulence gene is capable of expressing a gene product that facilitate invasion and colonization of the gut associated lymphoid tissues. (II) is useful for immunizing a human. (III) is useful for preparing a vaccine (claimed). (I) is useful to deliver and produce pharmacological active products that stimulate or suppress various physiological functions. The live attenuated bacteria is useful in vaccines to prevent diseases caused by various bacteria, viral, fungal, and protozoal pathogens and as delivery vehicles for genes and gene products. The strains are useful as carrier microorganisms for the production of expression products encoded on recombinant genes in bacterial cells, and in safety and improved immunogenicity against recombinant antigens.

ADMINISTRATION - Vaccine is administered by oral ingestion, gastric intubation or broncho-nasal-ocular spraying. No dosage details given. EXAMPLE - Construction of Salmonella strain was as follows: X3339 was a wild-type, virulent, animal-passaged isolate of *S.typhimurium* strain SL1344. SF1005 was an *rpoS::RR10* mutant derived from *S.typhimurium* strain American type culture collection (ATCC) 14028s and contained an ampicillin resistance gene linked to the *rpoS::RR10* mutant allele. The mutant *rpoS::RR10* allele was moved into X3339 using a P22HTint transducing phage lysate prepared on SF1005 and selected for ampicillin resistance (Apr) due to the presence of the beta-lactamase gene linked to the RR10 insertion in the *rpoS* gene. The allelic exchange between SF1005 and X3339 was confirmed by Southern blot analysis, and the resulting 3339 *rpoS::RR10* mutant derivative was designated as X4973. Transductants were screened for sensitivity to P22HTint by cross streaking with 22H5, a clear plaque mutant. Pseudolysogenic colonies were distinguished from non-lysogens on Evans blue and uranine (EBU) indicator agar. Media were supplemented with 50 microg ampicillin/ml when required to select for X4973. (53 pages)

CLASSIFICATION: PHARMACEUTICALS, Vaccines; GENETIC TECHNIQUES and APPLICATIONS, Gene Expression Techniques and Analysis; DISEASE, HIV and Other Virus Infections; DISEASE, Infectious Disease (non-viral)

CONTROLLED TERMS: PLASMID PCMV-BETA-MEDIATED SALMONELLA  
 TYPHIMURIUM RPOS+, MUTANT PAB, PUR, ARO,  
 ASD, DAP, NADA, PNCB, GALE, PMI, FUR, RPSL, OMPR,  
 HTRA, HEMA, CDT, CYA, CRP, DAM, PHOP, PHOQ, RFC, POXA, GALU,  
 METL, METH, MVIA, SODC, RECA, SSRA, SSRB, SIRA, SIRB, SIRC,  
 INV, HILA, HILC, HILD, RPOE, FLGM, TONB, SLYA,  
 TUMOR-ASSOCIATED ANTIGEN, AMPICILLIN-RESISTANCE GENE  
 TRANSFER, EXPRESSION IN SALMONELLA SP., HUMAN IMMUNIZATION,  
 SOUTHERN BLOT HYBRIDIZATION, APPL. BACTERIUM INFECTION, VIRUS  
 INFECTION, FUNGUS INFECTION, PROTOZOON INFECTION THERAPY,  
 ATTENUATED RECOMBINANT VACCINE ANTIBIOTIC-RESISTANCE  
 MAMMAL ANIMAL ANTISEPTIC VIRUCIDE (22, 30)

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ACCESSION NUMBER: 1997:37222 SCISEARCH Full-text

THE GENUINE ARTICLE: WA729

TITLE: Display of heterologous proteins on the surface of  
 microorganisms: From the screening of combinatorial  
 libraries to live recombinant vaccines

AUTHOR: Georgiou G (Reprint)  
 CORPORATE SOURCE: UNIV TEXAS, DEPT CHEM ENGN, AUSTIN, TX 78712 (Reprint)  
 AUTHOR: Stathopoulos C; Daugherty P S; Nayak A R; Iverson B L; Curtiss R  
 CORPORATE SOURCE: WASHINGTON UNIV, DEPT BIOL, ST LOUIS, MO 63130; UNIV TEXAS, DEPT CHEM & BIOCHEM, AUSTIN, TX 78712  
 COUNTRY OF AUTHOR: USA  
 SOURCE: NATURE BIOTECHNOLOGY, (JAN 1997) Vol. 15, No. 1, pp. 29-34  
 .  
 ISSN: 1087-0156.  
 PUBLISHER: NATURE PUBLISHING CO, 345 PARK AVE SOUTH, NEW YORK, NY 10010-1707.  
 DOCUMENT TYPE: General Review; Journal  
 FILE SEGMENT: LIFE; AGRI  
 LANGUAGE: English  
 REFERENCE COUNT: 90  
 ENTRY DATE: Entered STN: 1997  
 Last Updated on STN: 1997

## ABSTRACT:

In recent years there has been considerable progress towards the development of expression systems for the display of heterologous polypeptides and, to a lesser extent, oligosaccharides on the surface of bacteria or yeast. The availability of protein display vectors has in turn provided the impetus for a range of exciting technologies. Polypeptide libraries can be displayed in bacteria and screened by cell sorting techniques, thus simplifying the isolation of proteins with high affinity for ligands. Expression of antigens on the surface of nonvirulent microorganisms is an attractive approach to the development of high-efficacy recombinant live vaccines. Finally, cells displaying protein receptors or antibodies are of use for analytical applications and bioseparations.

CATEGORY: BIOTECHNOLOGY & APPLIED MICROBIOLOGY  
 SUPPLEMENTARY TERM: protein display; library screening; live bacterial vaccines  
 SUPPL. TERM PLUS: GRAM-NEGATIVE BACTERIA; RANDOM PEPTIDE LIBRARIES; MOUTH-DISEASE VIRUS; COLI CELL-SURFACE; ESCHERICHIA-COLI; OUTER-MEMBRANE; SALMONELLA-TYPHIMURIUM; IMMUNE-RESPONSES; ATTENUATED SALMONELLA; FOREIGN POLYPEPTIDES

## REFERENCE(S):

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG  (RPG)	Referenced Work (RWK)
ADEY N B	1995	156	27	GENE
AGTERBERG M	1990	88	37	GENE
AGTERBERG M	1990	8	438	VACCINE
BODER E T	1996			UNPUB SURFACE DISPLA
BONNYCASTLE L L C	1996	258	747	J MOL BIOL
BROWN S	1992	89	8651	P NATL ACAD SCI USA
BURTON D R	1994	57	191	ADV IMMUNOL
CARDENAS L	1992	5	328	CLIN MICROBIOL REV
CHARBIT A	1988	70	181	GENE
CHARBIT A	1987	139	1644	J IMMUNOL
CHEN G	1996	12	572	BIOTECHNOL PROGR
CHOO Y	1994	91	11163	P NATL ACAD SCI USA
CIRILLO J D	1995	20	1001	CLIN INFECT DIS
COLAS P	1996	380	548	NATURE
CORNELIS P	1996	14	203	BIO-TECHNOL
CRAMERI A	1996	2	100	NAT MED
CURTISS R	1996		499	ESSENTIALS MUCOSAL I
CURTISS R	1990		161	NEW GENERATION VACCI

CURTISS R	1990	8	237	TRENDS BIOTECHNOL
DAUGHERTY P	1997			UNPUB ISOLATION HIGH
DUNNE M	1995	63	1611	INFECT IMMUN
FISCHETTI V A	1996	62	405	ASM NEWS
FORMAL S B	1981	34	746	INFECT IMMUN
FORTAINE A	1990	141	907	RES MICROBIOL
FRANCISCO J A	1992	89	2713	P NATL ACAD SCI USA
FRANCISCO J A	1993	90	10444	P NATL ACAD SCI USA
FREEMAN A	1996	52	625	BIOTECHNOL BIOENG
FUCHS P	1991	9	1369	BIO-TECHNOL
GEORGIOU G	1996	9	239	PROTEIN ENG
GEORGIOU G	1993	11	6	TRENDS BIOTECHNOL
GODING J W	1978	20	241	J IMMUNOL METHODS
GOLDBERG J B	1992	89	10716	P NATL ACAD SCI USA
GRIFFITHS A D	1993	12	725	EMBO J
HANSSON M	1992	174	4239	J BACTERIOL
HARRISON J L	1996	267	109	METHOD ENZYMOL
HESS J	1996	93	1458	P NATL ACAD SCI USA
HILL R H	1996	20	685	MOL MICROBIOL
HOFNUNG M	1991	34	77	METHOD CELL BIOL
JAHNSCHMID B	1996	44	225	J BIOTECHNOL
JANSSEN R	1994	12	406	VACCINE
JOSE J	1995	18	378	MOL MICROBIOL
KLAUSER T	1993	15	799	BIOESSAYS
KLAUSER T	1990	9	1991	EMBO J
KNAPPIK A	1995	8	81	PROTEIN ENG
KORNACKER M G	1990	4	1101	MOL MICROBIOL
LAUKKANEN M L	1993	6	449	PROTEIN ENG
LEARY J F	1995	2678	240	SPIE
LECLERC C	1989	7	242	VACCINE
LITTLE M	1993	11	3	TRENDS BIOTECHNOL
LOWMAN H B	1993	234	564	J MOL BIOL
LU Z J	1995	13	366	BIO-TECHNOL
MARKLAND W	1996	35	8045	BIOCHEMISTRY-US
MATTHEWS D J	1993	260	113	SCIENCE
MEDAGLINI D	1995	92	6868	P NATL ACAD SCI USA
MESSNER P	1992	233	175	CARBOHYD RES
NEWTON S M C	1996	178	3447	J BACTERIOL
NEWTON S M C	1995	146	203	RES MICROBIOL
NEWTON S M C	1989	244	70	SCIENCE
OCALLAGHAN D	1990	141	963	RES MICROBIOL
PALLESEN L	1995	141	2839	MICROBIOL-UK
POZZI G	1992	60	1902	INFECT IMMUN
PROVENCE D L	1997			UNPUB ANAL EXTRACELL
RANTAMAKI L K	1995	45	115	VET IMMUNOL IMMUNOP
RENAULDMONGENIE G	1996	93	7944	P NATL ACAD SCI USA
ROBERTS M	1994		27	NOVEL DELIVERY SYSTE
RUPPERT A	1994	12	492	VACCINE
RYD M	1992	12	399	MICROB PATHOGENESIS
SALMOND G P C	1993	18	7	TRENDS BIOCHEM SCI
SAMUELSON P	1995	177	1470	J BACTERIOL
SCHORR J	1991	9	675	VACCINE
SCHREUDER M P	1996	14	383	VACCINE
SCHREUDER M P	1993	9	399	YEAST
SCOTT J K	1990	249	386	SCIENCE
SHORT M K	1995	270	28541	J BIOL CHEM
SHREUDER M P	1996	14	115	TRENDS BIOTECHNOL
SOUSA C	1996	14	1017	NAT BIOTECHNOL
STATHOPOULOS C	1996	45	112	APPL MICROBIOL BIOT
STEIDLER L	1993	175	7639	J BACTERIOL

STEVENSON G	1985	28	317	FEMS MICROBIOL LETT
STGEME J W	1994	14	217	MOL MICROBIOL
SU G F	1992	60	3345	INFECT IMMUN
SUZUKI T	1995	270	30874	J BIOL CHEM
TANG Y	1996	271	15682	J BIOL CHEM
TAYLOR I M	1990	4	1259	MOL MICROBIOL
VANDEVERG L	1990	58	2002	INFECT IMMUN
VANDIE I	1990	222	297	MOL GEN GENET
WANG C I	1996	267	28	METHOD ENZYMOL
WHITEHORN E A	1995	13	1215	BIO-TECHNOL
WONG R S Y	1995	158	55	GENE
YANG W P	1995	254	392	J MOL BIOL

L128 ANSWER 30 OF 39 SCISEARCH COPYRIGHT (c) 2010 The Thomson Corporation on  
STN

ACCESSION NUMBER: 1991:17834 SCISEARCH Full-text

THE GENUINE ARTICLE: EQ001

TITLE: CONTROL OF COLONIZATION BY VIRULENT SALMONELLA-  
TYPHIMURIUM BY ORAL IMMUNIZATION OF CHICKENS WITH  
AVIRULENT DELTA-CYA DELTA-CRP SALMONELLA-  
TYPHIMURIUM

AUTHOR: HASSAN J O (Reprint); CURTISS F

CORPORATE SOURCE: WASHINGTON UNIV, DEPT BIOL, ST LOUIS, MO 63130

COUNTRY OF AUTHOR: USA

SOURCE: RESEARCH IN MICROBIOLOGY, (SEP-OCT 1990) Vol. 141, No.  
7-8, pp. 839-850.  
ISSN: 0923-2508.

PUBLISHER: EDITIONS SCIENTIFIQUES ELSEVIER, 141 RUE JAVEL, 75747  
PARIS CEDEX 15, FRANCE.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: English

REFERENCE COUNT: 34

ENTRY DATE: Entered STN: 1994

Last Updated on STN: 1994

#### ABSTRACT:

Oral immunization with a DELTA-cya DELTA-crp Salmonella \*\*\*typhimurium\*\*\* strain has been shown to preclude colonization by wild-type, virulent S. typhimurium and induces humoral and cellular immune response in chickens. Intestinal tract colonization by the virulent challenge strain was used to determine the level of protection conferred by immunization with the DELTA-cya DELTA-crp mutant. The associated humoral and cellular immune responses were measured by ELISA and delayed-type hypersensitivity (DTH) tests, respectively. The levels of colonization by both Salmonella strains were determined by enumeration of viable cells in the intestinal tract. A reduction in faecal excretion of the wild-type strain was observed with a single oral immunization with the DELTA-cya DELTA-crp \*\*\*mutant\*\*\*, but caecal colonization was not affected. However, double oral immunization with the DELTA-cya DELTA-crp mutant precludes caecal colonization by the virulent strain. IgM, IgA and IgG were detected against sonicated Salmonella whole-cell antigens. Outer \*\*\*membrane\*\*\* and flagella proteins induced DTH responses, whereas lipopolysaccharide failed to do so. The effectiveness of the DELTA-cya DELTA-crp strain in reducing caecal colonization by the highly virulent challenge strain in chickens demonstrates that oral vaccination with the DELTA-cya DELTA-crp S. typhimurium should aid in eliminating Salmonella carriers in chickens. The elimination of these carriers on the poultry farm should help to control Salmonella contamination of poultry products, thereby improving public health.

CATEGORY: MICROBIOLOGY

SUPPLEMENTARY TERM: SALMONELLA-TYPHIMURIUM; IMMUNIZATION;  
 COLONIZATION; IMMUNE RESPONSES; CHICKENS; VACCINE  
 SUPPL. TERM PLUS: INFECTED CHICKENS; CECAL MICROFLORA; FECAL EXCRETION;  
 IMMUNITY; MUTANTS; RESISTANCE; PROTECTION;  
 VACCINES

## REFERENCE(S):

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
BARROW, P A	1988	17	571	AVIAN PATHOL
BARROW, P A	1990	104	413	EPIDEMIOL INFECT
BARROW, P A	1987	42	194	RES VET SCI
BROWN, D D	1975	18	165	RES VET SCI
COLLINS, F M	1974	38	371	BACTERIOL REV
CURTISS, R	1990			IN PRESS COLONIZATIO
CURTISS, R	1968	58	9	INFECT IMMUN
CURTISS, R	1965	89	28	J BACTERIOL
DAVIS, R W	1980			MANUAL GENETIC ENG A
DORMAN, C J	1989	57	2136	INFECT IMMUN
GALAN, J E	1989	6	433	MICROB PATHOGENESIS
GERMANIER, R	1971	4	663	INFECT IMMUN
HASSAN, J O	1990			IN PRESS COLONIZATIO
HASSAN, J O	1990	126	519	VET REC
HOISETH, S K	1981	291	238	NATURE
IMPEY, C S	1989	66	469	J APPL BACTERIOL
KITA, E	1984	87	528	CELL IMMUNOL
KITA, E	1987	61	535	IMMUNOLOGY
LEIFSON, E	1936	24	4423	AM J HYG
LENNOX, E S	1955	1	190	VIROLOGY
LOCKMAN, H A	1990	58	137	INFECT IMMUN
LURIA, S E	1957	74	461	J BACTERIOL
MALOY, S R	1981	145	1110	J BACTERIOL
MILES, A A	1938	38	732	J HYG CAMB
NEWELL, D G	1984	130	1201	J GEN MICROBIOL
ROBERTSSON, J A	1982	33	221	RES VET SCI
SCHMIEGER, H	1972	119	75	MOL GEN GENET
SEUNA, E	1979	58	1171	POULTRY SCI
SMITH, H W	1975	75	275	J HYG CAMB
SMITH, H W	1980	84	479	J HYG-CAMBRIDGE
SMYSER, C F	1966	10	314	AVIAN DIS
THAIN, J A	1978	102	143	VET REC
WIERUP, M	1985		94	P INT S SALMONELLA N
WILLIAMS, J E	1978		135	DISEASES POULTRY

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ACCESSION NUMBER: 2010424137 EMBASE Full-text

TITLE: Live recombinant Salmonella typhi vaccines constructed to investigate the role of rpoS in eliciting immunity to a heterologous antigen.

AUTHOR: Shi, Huoying; Santander, Javier; Brenneman, Karen E.; Wanda, Soo-Young; Wang, Shifeng; Senechal, Patti; Sun, Wei; Roland, Kenneth L.; Curtiss III, Roy

CORPORATE SOURCE: Center for Infectious Diseases and Vaccinology, The Biodesign Institute and School of Life Sciences, Arizona State University, Tempe, AZ, United States. rcurtiss@asu.edu

AUTHOR: Curtiss, R. (correspondence)

CORPORATE SOURCE: Center for Infectious Diseases and Vaccinology, The Biodesign Institute and School of Life Sciences, Arizona

State University, Tempe, AZ, United States. rcurtiss@asu.edu  
 SOURCE: PLoS ONE, (2010) Vol. 5, No. 6. arn. e11142.  
 Refs: 103  
 E-ISSN: 1932-6203  
 PUBLISHER: Public Library of Science, 185 Berry Street, Suite 1300,  
 San Francisco, CA 94107, United States.  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 026 Immunology, Serology and Transplantation  
 037 Drug Literature Index  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 30 Aug 2010  
 Last Updated on STN: 15 Nov 2010

ABSTRACT: We hypothesized that the immunogenicity of live *Salmonella enterica* serovar Typhi vaccines expressing heterologous antigens depends, at least in part, on its *rpoS* status. As part of our project to develop a recombinant \*\*\*attenuated\*\*\* *S. Typhi* vaccine (RASTyV) to prevent pneumococcal diseases in infants and children, we constructed three RASTyV strains synthesizing the *Streptococcus pneumoniae* surface protein PspA to test this hypothesis. Each vector strain carried ten engineered mutations designed to optimize safety and immunogenicity. Two *S. Typhi* vector strains (x9639 and x9640) were derived from the *rpoS* mutant strain Ty2 and one (x9633) from the *RpoS*+ strain ISP1820. In x9640, the nonfunctional *rpoS* gene was replaced with the functional *rpoS* gene from ISP1820. Plasmid pYA4088, encoding a secreted form of PspA, was moved into the three vector strains. The resulting RASTyV strains were evaluated for safety in vitro and for immunogenicity in mice. All three RASTyV strains were similar to the live attenuated typhoid vaccine Ty21a in their ability to survive in human blood and human monocytes. They were more sensitive to complement and were less able to survive and persist in sewage and surface water than their wild-type counterparts. Adult mice intranasally immunized with any of the RASTyV strains developed immune responses against PspA and *Salmonella* antigens. The *RpoS*+ vaccines induced a balanced Th1/Th2 immune response while the *RpoS*- strain x9639(pYA4088) induced a strong Th2 immune response. Immunization with any RASTyV provided protection against *S. pneumoniae* challenge; the *RpoS*+ strain x9640(pYA4088) provided significantly greater protection than the ISP1820 derivative, x9633(pYA4088). In the pre-clinical setting, these strains exhibited a desirable balance between safety and immunogenicity and are currently being evaluated in a Phase 1 clinical trial to determine which of the three RASTyVs has the optimal safety and immunogenicity profile in human hosts. .COPYRGHT. 2010 Shi et al.

CONTROLLED TERM: Medical Descriptors:  
 animal experiment  
 animal model  
 antigen expression  
 article  
 bacterial gene  
 bacterial strain  
 bacterial survival  
 bacterium mutant  
 blood  
 cellular immunity  
 complement system  
 controlled study  
 drug safety  
 female  
 hypothesis  
 immunization



\*immunogenicity  
 male  
 monocyte  
 newborn  
 nonhuman  
 plasmid  
 pneumococcal infection  
     *Salmonella typhi*  
 serotype  
 sewage  
 Th1 cell  
 Th2 cell

CONTROLLED TERM: Drug Descriptors:  
 bacterial antigen  
 membrane protein  
 recombinant vaccine  
 \*sigma factor RpoS  
 Streptococcus antigen  
 surface water  
 \*typhoid vaccine: NA, intranasal drug administration  
 \*typhoid vaccine: PO, oral drug administration

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ACCESSION NUMBER: 2010492342 EMBASE Full-text  
 TITLE: Delivery of woodchuck hepatitis virus-like particle presented influenza M2e by recombinant attenuated *Salmonella* displaying a delayed lysis phenotype.  
 AUTHOR: Ameiss, Keith; Ashraf, Shamaila; Kong, Wei; Curtiss, Roy (correspondence)  
 CORPORATE SOURCE: The Biodesign Institute, Center for Infectious Diseases and Vaccinology, Arizona State University, Tempe, AZ 85287, United States. rcurtiss@asu.edu  
 AUTHOR: Curtiss, Roy (correspondence)  
 CORPORATE SOURCE: School of Life Sciences, Arizona State University, Tempe, AZ 85287, United States. rcurtiss@asu.edu  
 AUTHOR: Pekosz, Andrew; Wu, Wai-Hong  
 CORPORATE SOURCE: Harry Feinstone Dept. of Molecular Microbiology and Immunology, Johns Hopkins Univ. Bloomberg School of Public Health, 615 North Wolfe Street, Suite E5132, Baltimore, MD 21205-2103, United States.  
 AUTHOR: Milich, David; Billaud, Jean-Noel  
 CORPORATE SOURCE: The Vaccine Research Institute of San Diego, 10835 Road to the Cure, Suite 150, San Diego, CA 92121, United States.  
 AUTHOR: Billaud, Jean-Noel  
 CORPORATE SOURCE: Ingenuity Systems, Redwood City, CA, United States.  
 AUTHOR: Ameiss, Keith  
 CORPORATE SOURCE: Pfizer Animal Health, Poultry Health Division, Durham, NC, United States.  
 AUTHOR: Curtiss, Roy (correspondence)  
 CORPORATE SOURCE: The Biodesign Institute, Arizona State University, P. O. Box 875401, Tempe, AZ 85287-5401, United States. rcurtiss@asu.edu  
 SOURCE: Vaccine, (September 2010) Vol. 28, No. 41, pp. 6704-6713. Refs: 56  
 ISSN: 0264-410X CODEN: VACCDE  
 PUBLISHER: Elsevier Ltd, Langford Lane, Kidlington, Oxford, OX5 1GB, United Kingdom.  
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 COUNTRY: United Kingdom

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 FILE SEGMENT: 004 Microbiology: Bacteriology, Mycology, Parasitology  
 and Virology  
 005 General Pathology and Pathological Anatomy  
 026 Immunology, Serology and Transplantation  
 037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 6 Oct 2010

Last Updated on STN: 6 Oct 2010

ABSTRACT: The use of live recombinant attenuated Salmonella vaccines (RASV) is a promising approach for controlling infections by multiple pathogens. The highly conserved extracellular domain of the influenza M2 protein (M2e) has been shown to provide broad spectrum protection against multiple influenza subtypes sharing similar M2e sequences. An M2e epitope common to a number of avian influenza subtypes was inserted into the core antigen of woodchuck hepatitis virus and expressed in two different recombinant \*\*\*attenuated\*\*\* Salmonella Typhimurium strains. One strain was \*\*\*attenuated\*\*\* via deletion of the cya and crp genes. The second strain was engineered to exhibit a programmed delayed lysis phenotype. Both strains were able to produce both monomeric fusion proteins and fully assembled core particles. Mice orally immunized with the strain exhibiting delayed lysis induced significantly greater antibody titers than the  $\Delta cya \Delta crp$  strain and provided moderate protection against weight loss to a low level challenge with the influenza strain A/WSN/33 modified to express the M2e sequence common to avian viruses. Further studies indicated that the Salmonella expressed core antigen induced comparable antibody levels to the purified core antigen injected with an alum adjuvant and that both are able to reduce viral replication in the lungs. To our knowledge this is the first report demonstrating Salmonella-mediated delivery of influenza virus M2e protein in a mammalian host to induce a protective immune response against viral challenge. .COPYRGT. 2010 Elsevier Ltd.

CONTROLLED TERM: Medical Descriptors:  
 animal experiment  
 animal model  
 antibody titer  
 article  
 avian influenza: DT, drug therapy  
 bacterial gene  
 bacterial strain  
 controlled study  
 crp gene  
 cya gene  
 DNA modification  
   gene deletion  
 genetic engineering  
 immune response  
 lysis  
 mouse  
 nonhuman  
 phenotype  
 priority journal  
 protein expression  
   \*Salmonella  
   Salmonella typhimurium  
 sequence analysis  
 viral gene delivery system  
 virus like agent  
 virus replication

CONTROLLED TERM: \*Woodchuck hepatitis virus  
 Drug Descriptors:  
 aluminum potassium sulfate  
 epitope  
 hybrid protein  
 \*protein M2: DT, drug therapy  
 \*recombinant attenuated salmonella vaccine: DT, drug  
 therapy  
 \*salmonellosis vaccine: DT, drug therapy  
 unclassified drug  
 SUPPLEMENTARY TERM: Influenza; M2e; RASV; Salmonella; Virus-like particle  
 CAS REGISTRY NO.: (aluminum potassium sulfate) 10043-67-1

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ACCESSION NUMBER: 2010436326 EMBASE Full-text  
 TITLE: Regulated delayed expression of rfc enhances the immunogenicity and protective efficacy of a heterologous antigen delivered by live attenuated Salmonella enterica vaccines.  
 AUTHOR: Kong, Qingke; Liu, Qing; Jansen, Angela M.; Curtiss, Roy (correspondence)  
 CORPORATE SOURCE: Center for Infectious Diseases and Vaccinology, The Biodesign Institute and School of Life Sciences, Arizona State University, Tempe, AZ 85287, United States. rcurtiss@asu.edu  
 AUTHOR: Curtiss, Roy (correspondence)  
 CORPORATE SOURCE: Center for Infectious Diseases and Vaccinology, The Biodesign Institute, Arizona State University, PO Box 875401, 1001 S. McAllister Avenue, Tempe, AZ 85287-5401, United States. rcurtiss@asu.edu  
 SOURCE: Vaccine, (August 2010) Vol. 28, No. 37, pp. 6094-6103. Refs: 50  
 ISSN: 0264-410X CODEN: VACCDE  
 PUBLISHER: Elsevier Ltd, Langford Lane, Kidlington, Oxford, OX5 1GB, United Kingdom.  
 PUBLISHER IDENT.: S 0264-410X(10)00902-3  
 COUNTRY: United Kingdom  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 004 Microbiology: Bacteriology, Mycology, Parasitology and Virology  
 030 Clinical and Experimental Pharmacology  
 037 Drug Literature Index  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 2 Sep 2010  
 Last Updated on STN: 2 Sep 2010

ABSTRACT: The Salmonella rfc gene encodes the O-antigen polymerase. We constructed three strains in which we replaced the native rfc promoter with the arabinose-dependent araC PBAD promoter so that rfc expression was dependent on exogenously supplied arabinose provided during in vitro growth. The three mutant strains were designed to synthesize different amounts of Rfc by altering the ribosome-binding sequence and start codon. We examined these strains for a number of in vitro characteristics compared to an isogenic  $\Delta$ rfc mutant and the wild-type parent strain. One promoter-replacement mutation,  $\Delta$ Prfc174, yielded an optimal profile, exhibiting wild-type characteristics when grown with arabinose, and  $\Delta$ rfc characteristics when grown without arabinose. In addition, when administered orally, the  $\Delta$ Prfc174 strain was completely attenuated in for virulence in

mice. The  $\Delta$ Prfc174 mutation was introduced into attenuated *Salmonella* vaccine strain  $\chi$ 9241 ( $\Delta$ pabA  $\Delta$ pabB  $\Delta$ asdA) followed by introduction of an Asd<sup>+</sup> balanced-lethal plasmid to designed for expression of the pneumococcal surface protein PspA. Mice immunized with either  $\chi$ 9241 or its  $\Delta$ Prfc174 derivative expressing pspA were protected against *S. pneumoniae* challenge. .COPYRG. 2010.

CONTROLLED TERM: Medical Descriptors:  
 animal experiment  
 animal model  
 animal tissue  
 article  
     bacterial mutation  
 bacterial strain  
 bacterial virulence  
     bacterium mutant  
 codon  
 controlled study  
 drug delivery system  
 drug efficacy  
 female  
 immunogenicity  
 in vitro study  
     microbial attenuation  
 mouse  
 nonhuman  
 plasmid  
 \*pneumococcal infection  
 priority journal  
 protein expression  
 ribosome

            \**Salmonella enterica*  
     \*salmonellosis  
 Streptococcus pneumoniae  
 CONTROLLED TERM: Drug Descriptors:  
 arabinose  
 \*bacterial protein  
 \*pneumococcal surface protein  
 \*protein RFC  
 \*typhoid vaccine: PO, oral drug administration  
 \*typhoid vaccine: PD, pharmacology  
 unclassified drug

SUPPLEMENTARY TERM: Arabinose-regulated rfc expression; PspA

CAS REGISTRY NO.: (arabinose) 147-81-9

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ACCESSION NUMBER: 2010438288 EMBASE Full-text

TITLE: Evaluation of the humoral immune response in mice orally vaccinated with live recombinant attenuated *Salmonella enterica* delivering a secreted form of *Yersinia pestis* PsaA.

AUTHOR: Torres-Escobar, Ascencion; Juarez-Rodriguez, Maria Dolores; Branger, Christine G.; Curtiss, Roy  
 (correspondence)

CORPORATE SOURCE: Center for Infectious Disease and Vaccinology, Biodesign Institute and School of Life Sciences, Arizona State University, Tempe, AZ 85287-5401, United States. rcurtiss@asu.edu

AUTHOR: Curtiss, Roy (correspondence)  
 CORPORATE SOURCE: The Biodesign Institute, Center for Infectious Diseases and Vaccinology, Arizona State University, PO Box 875401, 1001 S. McAllister Avenue, Tempe, AZ 85287-5401, United States. rcurtiss@asu.edu  
 SOURCE: Vaccine, (August 2010) Vol. 28, No. 36, pp. 5810-5816.  
 Refs: 55  
 ISSN: 0264-410X CODEN: VACCDE  
 PUBLISHER: Elsevier Ltd, Langford Lane, Kidlington, Oxford, OX5 1GB, United Kingdom.  
 PUBLISHER IDENT.: S 0264-410X(10)00898-4  
 COUNTRY: United Kingdom  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 004 Microbiology: Bacteriology, Mycology, Parasitology and Virology  
 026 Immunology, Serology and Transplantation  
 037 Drug Literature Index  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 30 Aug 2010  
 Last Updated on STN: 30 Aug 2010  
 ABSTRACT: *Yersinia pestis* PsaA is an adhesin that is synthesized inside macrophages. Here, we evaluated the immune profile of codon-optimized *Y. pestis* PsaA synthesized in a live recombinant attenuated *Salmonella* vaccine (RASV) strain  $\chi$ 9558. Oral immunization of BALB/c mice with  $\chi$ 9558(pYA3705) delivering a secreted form of PsaA, elicited a systemic PsaA-specific immunoglobulin G (IgG) response but offered limited protection against lethal challenge with the intranasally introduced *Y. pestis* CO92 strain. Our results suggest that appropriate fine-tuning of *Y. pestis* PsaA delivery by RASV could improve its protective role in curtailing plague colonization and infection. .COPYRG. 2010 Elsevier Ltd.

CONTROLLED TERM: Medical Descriptors:  
 animal experiment  
 antibody production  
 article  
 bacterial colonization  
 bacterial strain  
 codon  
 controlled study  
 female  
 \*humoral immunity  
   indel mutation  
 mouse  
 mucosal immunity  
 nonhuman  
 priority journal  
 protection  
 protein stability  
   *Salmonella typhimurium*  
 survival  
*Yersinia pestis*  
 \*yersiniosis: DT, drug therapy  
 \*yersiniosis: PC, prevention

CONTROLLED TERM: Drug Descriptors:  
 \*bacterial protein: DV, drug development  
 \*bacterial protein: DT, drug therapy  
 \*bacterial protein: PO, oral drug administration  
 \*bacterial protein: PD, pharmacology  
 \*bacterial vaccine: DT, drug therapy

\*bacterial vaccine: PO, oral drug administration  
 \*bacterial vaccine: PD, pharmacology  
 immunoglobulin A antibody: EC, endogenous compound  
 immunoglobulin G1 antibody: EC, endogenous compound  
 immunoglobulin G2a antibody: EC, endogenous compound  
 \*live vaccine: DT, drug therapy  
 \*live vaccine: PO, oral drug administration  
 \*live vaccine: PD, pharmacology  
 \*protein psaa: DV, drug development  
 \*protein psaa: DT, drug therapy  
 \*protein psaa: PO, oral drug administration  
 \*protein psaa: PD, pharmacology  
 unclassified drug

SUPPLEMENTARY TERM: Asd+; Codon-optimized; PsaA antigen; PsaB chaperone protein; PsaC usher protein; Vaccine plasmid

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ACCESSION NUMBER: 0011858870 EMBASE Full-text

COPYRIGHT: MEDLINE® is the source for the citation and abstract of this record.

TITLE: Immunogenicity of chi4127 phoP- Salmonella enterica serovar Typhimurium in dogs..

AUTHOR: McVey, D Scott (correspondence); Chengappa, M.M.; Mosier, Derek E; Stone, Gregory G; Oberst, Richard D; Sylte, Matt J; Gabbert, Nathan M; Kelly-Aehle, Sandra M; Curtiss, Roy

CORPORATE SOURCE: Department of Diagnostic Medicine and Pathobiology, College of Veterinary Medicine, Kansas State University, Manhattan, KS 66506, USA.. d\_scott\_mcvey@groton.pfizer.com

SOURCE: Vaccine, (22 Feb 2002) Vol. 20, No. 11-12, pp. 1618-1623. ISSN: 0264-410X

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: MEDLINE

LANGUAGE: English

ENTRY DATE: Entered STN: Mar 2010

Last Updated on STN: Mar 2010

ABSTRACT: Salmonellae are commonly isolated from dogs. The number of dogs infected with Salmonella spp. is surprisingly high and greater than the incidence of clinical disease would suggest. Salmonellosis is common in greyhound kennels. Morbidity can approach 100% in puppies and the mortality ranges to nearly 40%. To date, there has been little effort to evaluate the feasibility of a vaccine for control of this disease in dogs. In the studies described here, an attenuated strain of Salmonella enterica serovar Typhimurium (Se Typhimurium), chi4127, was capable of establishing a limited infection in dogs. The chi4127-attenuated salmonellae efficiently stimulated protective immune responses in serotype homologous, direct, oral challenge experiments. Morbidity in the wild-type-challenged dogs was 8.3% in immunized dogs but 100% in the non-vaccinated controls. In (9/12) control dogs, the disease involved both gastrointestinal and respiratory tracts with high fever (>40.2 degrees C) that persisted through 5 days after challenge. Serum IgG response against S. typhimurium lipopolysaccharide (LPS) significantly increased (P<0.01) in vaccinated dogs and in non-vaccinated dogs after challenge. The non-vaccinated dogs had 3 to 4 logs higher numbers of Se Typhimurium in splenic and hepatic tissue than did the vaccinated dogs. This particular attenuated strain has potential for use as a vaccine for canine salmonellosis.

CONTROLLED TERM: Medical Descriptors:

animal  
 animal disease  
 \*animal salmonellosis: PC, prevention  
 article  
 blood  
 classification  
 dog  
 gastrointestinal disease: PC, prevention  
 immunology  
 isolation and purification  
 mucosal immunity  
 respiratory tract disease: PC, prevention  
 \*Salmonella typhimurium  
 serotyping

CONTROLLED TERM: Drug Descriptors:  
 bacterium antibody  
 immunoglobulin G  
 live vaccine: PD, pharmacology  
 salmonellosis vaccine: PD, pharmacology  
 CAS REGISTRY NO.: (immunoglobulin G) 97794-27-9

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ACCESSION NUMBER: 0011348727 EMBASE Full-text  
 COPYRIGHT: MEDLINE® is the source for the citation and abstract of this record.  
 TITLE: Intranasal immunogenicity of a Deltacya Deltacrp-pabA mutant of Salmonella enterica serotype Typhimurium for the horse..  
 AUTHOR: Sheoran, A.S. (correspondence); Timoney, J.F.; Tinge, S.A.; Sundaram, P.; Curtiss, E.  
 CORPORATE SOURCE: Department of Veterinary Science, Gluck Equine Research Center, University of Kentucky, 40546-0099, Lexington, KY, USA.  
 SOURCE: Vaccine, (14 May 2001) Vol. 19, No. 25-26, pp. 3591-3599. ISSN: 0264-410X  
 COUNTRY: United Kingdom  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: MEDLINE  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: Mar 2010  
 Last Updated on STN: Mar 2010

ABSTRACT: The aim of this study was to investigate the intranasal immunogenicity for the horse of a Deltacya Deltacrp-pabA mutant (MGN-707) of Salmonella enterica serotype Typhimurium (*S. typhimurium*). MGN-707 caused no sign of disease, was not detected in feces and a single administration induced strong Salmonella-specific serum and nasal mucosal antibody responses. All ponies had made strong salmonella specific serum IgG<sub>a</sub>, IgG<sub>b</sub>, IgA and IgM antibody responses by day 25 after the first immunization. IgM responses to salmonella lipopolysaccharide (LPS) were short lived whereas salmonella specific serum IgG<sub>a</sub> and IgG<sub>b</sub> persisted at high levels in all ponies until 83 and 140 days, respectively. Specific nasal mucosal antibody responses dominated by IgA and IgM were evident by day 25 in all ponies except one in which only specific IgG<sub>a</sub> and IgG<sub>b</sub> were evident. Specific nasal mucosal IgA persisted in most ponies until day 69. A second immunization on day 140 boosted antibody responses, and stimulated a strong nasal mucosal IgA response in the pony that failed to make an IgA response after primary immunization. At the termination of the experiment, IgA and IgG<sub>b</sub> dominated jejunal antibody responses whereas vaginal responses were mainly IgA. The latter response unequivocally confirms the existence of a common mucosal immune system in

equids. The results indicate that a *S. typhimurium* Deltacya Deltacrp-pabA mutant has potential as an intranasal vaccine against salmonellosis in the horse.

CONTROLLED TERM: Medical Descriptors:  
 animal  
 animal salmonellosis: PC, prevention  
 article  
 bacterial gene  
 biosynthesis  
 blood  
 feces  
 female  
   gene deletion  
 genetics  
 horse  
 horse disease: PC, prevention  
 immunology  
 intranasal drug administration  
 microbiology  
 mucosal immunity  
   mutation  
 nucleotide sequence  
   \*Salmonella typhimurium  
 vagina

CONTROLLED TERM: Drug Descriptors:  
 adenylate cyclase  
 bacterial protein  
 \*bacterial vaccine: AD, drug administration  
 bacterium antibody  
 cyclic AMP receptor  
 \*Escherichia coli protein  
 \*lyase  
 PabA protein, E coli  
 primer DNA

CAS REGISTRY NO.: (adenylate cyclase) 9012-42-4; (lyase) 9055-04-3

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ACCESSION NUMBER: 0007958478 EMBASE Full-text  
 COPYRIGHT: MEDLINE® is the source for the citation and abstract of this record.

TITLE: Recombinant Salmonella vectors in vaccine development..  
 AUTHOR: Curtiss 3rd., R.; Kelly, S.M.; Tinge, S.A.; Tacket, C.O.; Levine, M.M.; Srinivasan, J.; Koopman, M.

CORPORATE SOURCE: Washington University, Department of Biology, St. Louis, MO..

AUTHOR: Curtiss, R. (correspondence)  
 CORPORATE SOURCE: Washington University, Department of Biology, St. Louis, MO..

SOURCE: Developments in biological standardization, (1994) Vol. 82, pp. 23-33.  
 Refs: 46  
 ISSN: 0301-5149

COUNTRY: Switzerland  
 DOCUMENT TYPE: Journal; General Review; (Review)  
 FILE SEGMENT: MEDLINE  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: Mar 2010  
 Last Updated on STN: Mar 2010



ABSTRACT: A diversity of means are available for the attenuation of Salmonella which can be used to immunize animals and humans orally to elicit mucosal, humoral and cellular immune responses. Avirulent Salmonellae can be genetically engineered to express foreign antigens and the recombinant avirulent Salmonellae are capable of stable, high-level expression of the foreign antigen in the orally immunized animal or human host. The resulting vaccines are safe, efficacious, and are easy and economical to use.

CONTROLLED TERM: Medical Descriptors:  
 animal  
 \*animal salmonellosis: PC, prevention  
 bacterial gene  
 biosynthesis  
     gene deletion  
 \*gene vector  
 genetic engineering  
 genetics  
 human  
 immunology  
 oral drug administration  
 pathogenicity  
 review  
     \*Salmonella  
 \*salmonellosis: PC, prevention  
 virulence

CONTROLLED TERM: Drug Descriptors:  
 bacterial antigen  
 \*bacterial vaccine: AD, drug administration  
 bacterium antibody  
     live vaccine  
 \*recombinant vaccine: AD, drug administration  
 typhoid paratyphoid vaccine: AD, drug administration

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ACCESSION NUMBER: 0002692430 EMBASE Full-text  
 COPYRIGHT: MEDLINE® is the source for the citation and abstract of this record.

TITLE: Stable recombinant avirulent Salmonella vaccine strains..  
 AUTHOR: Curtiss 3rd., R.; Kelly, S.M.; Gulig, P.A.; Nakayama, K.  
 CORPORATE SOURCE: Department of Biology, Washington University, St. Louis, MO 63130..  
 AUTHOR: Curtiss, R. (correspondence)  
 CORPORATE SOURCE: Department of Biology, Washington University, St. Louis, MO 63130..  
 SOURCE: Advances in experimental medicine and biology, (1989) Vol. 251, pp. 33-47.  
 Refs: 40  
 ISSN: 0065-2598

COUNTRY: United States  
 DOCUMENT TYPE: Journal; General Review; (Review)  
 FILE SEGMENT: MEDLINE  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: Mar 2010  
 Last Updated on STN: Mar 2010

CONTROLLED TERM: Medical Descriptors:  
 animal  
 chromosome deletion  
 genetics  
 human

immunology  
molecular cloning  
pathogenicity  
plasmid  
review  
\*Salmonella  
species difference

CONTROLLED TERM: Drug Descriptors:  
adenylate cyclase  
bacterial antigen  
\*bacterial vaccine  
cyclic AMP receptor  
live vaccine  
\*recombinant vaccine  
\*vaccine

CAS REGISTRY NO.: (adenylate cyclase) 9012-42-4

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ACCESSION NUMBER: 0003291452 EMBASE Full-text

COPYRIGHT: MEDLINE® is the source for the citation and abstract of this record.

TITLE: Avirulent Salmonella typhimurium delta cya delta crp oral vaccine strains expressing a streptococcal colonization and virulence antigen..

AUTHOR: Curtiss 3rd., R.; Goldschmidt, R.M.; Fletchall, N.B.; Kelly, S.M.

CORPORATE SOURCE: Department of Biology, Washington University, St. Louis, MO 63130..

AUTHOR: Curtiss, R. (correspondence)

CORPORATE SOURCE: Department of Biology, Washington University, St. Louis, MO 63130..

SOURCE: Vaccine, (Apr 1988) Vol. 6, No. 2, pp. 155-160.  
Refs: 41  
ISSN: 0264-410X

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: MEDLINE

LANGUAGE: English

ENTRY DATE: Entered STN: Mar 2010  
Last Updated on STN: Mar 2010

ABSTRACT: Salmonella typhimurium SR-11 strains lacking adenylate cyclase and the cyclic AMP receptor protein (CRP) due to deletion (delta) mutations in the cya and crp genes, respectively, are avirulent for mice and induce high level protective immunity against subsequent challenge with wild-type virulent S. typhimurium SR-11 cells. The avirulence of these delta cya delta crp mutants has been enhanced by elimination of the 100 kb virulence plasmid pStSR100 without impairing immunogenicity. The present report confirms the avirulence and immunogenicity of these mutant strains, demonstrates that immunization of both four- and eight-week-old mice has no adverse effect on weight gain, and that immunity lasts at least ninety days following initial immunization. Avirulent S. typhimurium strains have been endowed with the ability to produce several streptococcal colonization and virulence antigens for the purpose of constructing recombinant bivalent oral vaccine strains. Important antigenic determinants of the Streptococcus sobrinus surface protein antigen A (SpaA), presumed to be a critical colonization antigen of S. sobrinus, are expressed at high level by the delta cya delta crp S. typhimurium strains. The recombinant vaccine strains are stable in vitro and in animals (for a period of at least eight days) where they localize to the gut-associated lymphoid tissue (GALT).

CONTROLLED TERM: Medical Descriptors:  
animal  
bacterium transformation  
Bagg albino mouse  
female  
genetics  
immunology  
isolation and purification  
molecular genetics  
mouse  
nucleotide sequence  
oral drug administration  
pathogenicity  
plasmid  
review  
    \*Salmonella typhimurium  
virulence

CONTROLLED TERM: Drug Descriptors:  
bacterial antigen  
\*bacterial vaccine  
    live vaccine  
recombinant vaccine

## TEXT SEARCH

=> fil pascal biotechno wpix biosis dissabs lifesci esbio biotechds bioeng  
scisearch

FILE 'PASCAL' ENTERED AT 10:05:33 ON 30 NOV 2010

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FILE 'SCISEARCH' ENTERED AT 10:05:33 ON 30 NOV 2010

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=> d que l111; d que l113; d que l116

L99 249856 SEA SALMONELLA  
L100 8 SEA ((ARACP OR ARA CP) (W) BAD OR ARACPBAD OR ARA CPBAD)  
L111 8 SEA L99 AND L100

L99 249856 SEA SALMONELLA  
L101 1088 SEA FUR GENE#  
L102 1719 SEA FERRIC UPTAKE REGULAT?  
L103 13365 SEA O(W) ANTIGEN#  
L112 173 SEA L99 AND (L101 OR L102)  
L113 4 SEA L103 AND L112

L99 249856 SEA SALMONELLA  
L101 1088 SEA FUR GENE#  
L102 1719 SEA FERRIC UPTAKE REGULAT?  
L104 2667600 SEA MUTAT? OR MUTANT#  
L109 751214 SEA ATTENUAT?  
L115 89324 SEA OUTER MEMBRANE  
L116 7 SEA L99 AND (L101 OR L102) AND (L104 OR L109) AND L115

=> s 1111,1113,1116 not 1126

L129            12 (L111 OR L113 OR L116) NOT L126            L126=INVENTOR SEARCH

=> fil capl; d que 14; d que 18; d que 112; d que 118; d que 119; d que 121

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FILE COVERS 1907 - 30 Nov 2010 VOL 153 ISS 23  
 FILE LAST UPDATED: 29 Nov 2010 (20101129/ED)  
 REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2010  
 USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2010

CAPLUS now includes complete International Patent Classification (IPC) reclassification data for the fourth quarter of 2010.

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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L4            3 SEA FILE=CAPLUS SPE=ON ABB=ON ((ARACP OR ARA CP) (W)BAD OR ARACPBAD OR ARA CPBAD)/BI

L3            37998 SEA FILE=CAPLUS SPE=ON ABB=ON SALMONELLA/CW  
 L5            708 SEA FILE=CAPLUS SPE=ON ABB=ON GENE#/OBI (L)FUR/OBI OR (FUR GENE#)/BI  
 L7            51696 SEA FILE=CAPLUS SPE=ON ABB=ON ATTENUAT?/OBI  
 L8            10 SEA FILE=CAPLUS SPE=ON ABB=ON L3 AND L5 AND L7

L3            37998 SEA FILE=CAPLUS SPE=ON ABB=ON SALMONELLA/CW  
 L5            708 SEA FILE=CAPLUS SPE=ON ABB=ON GENE#/OBI (L)FUR/OBI OR (FUR GENE#)/BI  
 L9            38618 SEA FILE=CAPLUS SPE=ON ABB=ON LIPOPOLYSACCHARIDES/CT  
 L11           524 SEA FILE=CAPLUS SPE=ON ABB=ON L9 (L) SYNTHES?/OBI  
 L12           1 SEA FILE=CAPLUS SPE=ON ABB=ON L11 AND L3 AND L5

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L3      37998 SEA FILE=CAPLUS SPE=ON  ABB=ON  SALMONELLA/CW
L4      3 SEA FILE=CAPLUS SPE=ON  ABB=ON  ((ARACP OR ARA CP) (W)BAD OR
        ARACPBAD OR ARA CPBAD)/BI
L5      708 SEA FILE=CAPLUS SPE=ON  ABB=ON  GENE#/OBI(L)FUR/OBI OR (FUR
        GENE#)/BI
L15     3376 SEA FILE=CAPLUS SPE=ON  ABB=ON  O/OBI(L)ANTIGEN#/CW
L18     2 SEA FILE=CAPLUS SPE=ON  ABB=ON  L15 AND L3 AND (L4 OR L5)

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L3      37998 SEA FILE=CAPLUS SPE=ON  ABB=ON  SALMONELLA/CW
L9      38618 SEA FILE=CAPLUS SPE=ON  ABB=ON  LIPOPOLYSACCHARIDES/CT
L11     524 SEA FILE=CAPLUS SPE=ON  ABB=ON  L9(L)SYNTHES?/OBI
L15     3376 SEA FILE=CAPLUS SPE=ON  ABB=ON  O/OBI(L)ANTIGEN#/CW
L19     3 SEA FILE=CAPLUS SPE=ON  ABB=ON  L11 AND L15 AND L3

```

```

L3      37998 SEA FILE=CAPLUS SPE=ON  ABB=ON  SALMONELLA/CW
L7      51696 SEA FILE=CAPLUS SPE=ON  ABB=ON  ATTENUAT?/OBI
L9      38618 SEA FILE=CAPLUS SPE=ON  ABB=ON  LIPOPOLYSACCHARIDES/CT
L15     3376 SEA FILE=CAPLUS SPE=ON  ABB=ON  O/OBI(L)ANTIGEN#/CW
L21     6 SEA FILE=CAPLUS SPE=ON  ABB=ON  L3 AND L7 AND L15 AND L9

```

=> s 14,18,112,118,119,121 not 135

L130 10 (L4 OR L8 OR L12 OR L18 OR L19 OR L21) NOT L35

=> fil embase; d que 184; d que 185; d que 187; d que 190

FILE 'EMBASE' ENTERED AT 10:05:39 ON 30 NOV 2010  
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FILE COVERAGE: EMBASE-originated material 1947 to 26 Nov 2010 (20101126/ED)  
Unique MEDLINE content 1948 to present

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and biweekly.

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```

L84     1 SEA FILE=EMBASE SPE=ON  ABB=ON  ((ARACP OR ARA CP) (W)BAD OR
        ARACPBAD OR ARA CPBAD)

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L68     67092 SEA FILE=EMBASE SPE=ON  ABB=ON  SALMONELLA+NT/CT
L71     190 SEA FILE=EMBASE SPE=ON  ABB=ON  FUR GENE#
L85     7 SEA FILE=EMBASE SPE=ON  ABB=ON  L68 AND L71

```

```

L68     67092 SEA FILE=EMBASE SPE=ON  ABB=ON  SALMONELLA+NT/CT
L70     367 SEA FILE=EMBASE SPE=ON  ABB=ON  FERRIC UPTAKE REGULAT?

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L74 2711 SEA FILE=EMBASE SPE=ON ABB=ON O ANTIGEN/CT  
 L87 1 SEA FILE=EMBASE SPE=ON ABB=ON L68 AND L70 AND L74

L68 67092 SEA FILE=EMBASE SPE=ON ABB=ON SALMONELLA+NT/CT  
 L70 367 SEA FILE=EMBASE SPE=ON ABB=ON FERRIC UPTAKE REGULAT?  
 L78 11332 SEA FILE=EMBASE SPE=ON ABB=ON LIVE VACCINE/CT  
 L79 189362 SEA FILE=EMBASE SPE=ON ABB=ON ATTENUAT?  
 L80 544225 SEA FILE=EMBASE SPE=ON ABB=ON MUTATION+NT/CT  
 L81 48065 SEA FILE=EMBASE SPE=ON ABB=ON MUTANT/CT OR BACTERIUM  
 MUTANT+NT/CT  
 L82 31722 SEA FILE=EMBASE SPE=ON ABB=ON MUTANT PROTEIN/CT  
 L86 10 SEA FILE=EMBASE SPE=ON ABB=ON L68 AND L70 AND (L78 OR L79 OR  
 L80 OR L81 OR L82)  
 L89 11319 SEA FILE=EMBASE SPE=ON ABB=ON REGULATOR GENE/CT  
 L90 1 SEA FILE=EMBASE SPE=ON ABB=ON L86 AND L89

=> s 184,185,187,190 not 197

L131 10 (L84 OR L85 OR L87 OR L90) NOT L97 L97=INVENTOR SEARCH

=> fil medl; d que 138; d que 147; d que 150;d que 154; d que 155; d que 157

FILE 'MEDLINE' ENTERED AT 10:05:41 ON 30 NOV 2010

FILE LAST UPDATED: 27 Nov 2010 (20101127/UP). FILE COVERS 1946 TO DATE.

MEDLINE and LMEDLINE have been updated with the 2010 Medical Subject Headings (MeSH) vocabulary and tree numbers from the U.S. National Library of Medicine (NLM). Additional information is available at

[http://www.nlm.nih.gov/pubs/techbull/nd09/nd09\\_medline\\_data\\_changes\\_2010.html](http://www.nlm.nih.gov/pubs/techbull/nd09/nd09_medline_data_changes_2010.html).

The Medline file has been reloaded effective January 24, 2010. See HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

See HELP RANGE before carrying out any RANGE search.

L38 1 SEA FILE=MEDLINE SPE=ON ABB=ON ((ARACP OR ARA CP) (W)BAD OR  
 ARACPBAD OR ARA CPBAD)

L37 48420 SEA FILE=MEDLINE SPE=ON ABB=ON SALMONELLA+NT/CT  
 L43 154 SEA FILE=MEDLINE SPE=ON ABB=ON FUR GENE#  
 L47 5 SEA FILE=MEDLINE SPE=ON ABB=ON L43 AND L37

L39 2584 SEA FILE=MEDLINE SPE=ON ABB=ON O ANTIGENS/CT  
 L43 154 SEA FILE=MEDLINE SPE=ON ABB=ON FUR GENE#  
 L50 0 SEA FILE=MEDLINE SPE=ON ABB=ON L39 AND L43

```

L37      48420 SEA FILE=MEDLINE SPE=ON  ABB=ON  SALMONELLA+NT/CT
L39      2584 SEA FILE=MEDLINE SPE=ON  ABB=ON  O ANTIGENS/CT
L52      490 SEA FILE=MEDLINE SPE=ON  ABB=ON  FERRIC UPTAKE REGULATING
        PROTEINS, BACTERIAL/CN
L53      27 SEA FILE=MEDLINE SPE=ON  ABB=ON  L52 AND L37
L54      0 SEA FILE=MEDLINE SPE=ON  ABB=ON  L53 AND L39

```

```

L37      48420 SEA FILE=MEDLINE SPE=ON  ABB=ON  SALMONELLA+NT/CT
L40      7659 SEA FILE=MEDLINE SPE=ON  ABB=ON  VACCINES, ATTENUATED/CT
L52      490 SEA FILE=MEDLINE SPE=ON  ABB=ON  FERRIC UPTAKE REGULATING
        PROTEINS, BACTERIAL/CN
L55      1 SEA FILE=MEDLINE SPE=ON  ABB=ON  L52 AND L37 AND L40

```

```

L37      48420 SEA FILE=MEDLINE SPE=ON  ABB=ON  SALMONELLA+NT/CT
L52      490 SEA FILE=MEDLINE SPE=ON  ABB=ON  FERRIC UPTAKE REGULATING
        PROTEINS, BACTERIAL/CN
L56      20666 SEA FILE=MEDLINE SPE=ON  ABB=ON  BACTERIAL OUTER MEMBRANE
        PROTEINS+NT/CT
L57      1 SEA FILE=MEDLINE SPE=ON  ABB=ON  L52 AND L37 AND L56

```

=> s 138,147,155,157 not 166

```

L132      5 (L38 OR L47 OR L55 OR L57) NOT L66          L66=INVENTOR SEARCH

```

=> => dup rem 1132,1130,1129,1131

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PROCESSING COMPLETED FOR L132

PROCESSING COMPLETED FOR L130

PROCESSING COMPLETED FOR L129

PROCESSING COMPLETED FOR L131

L133 27 DUP REM L132 L130 L129 L131 (10 DUPLICATES REMOVED)



ANSWERS '1-5' FROM FILE MEDLINE  
 ANSWERS '6-15' FROM FILE CAPLUS  
 ANSWER '16' FROM FILE WPIX  
 ANSWERS '17-19' FROM FILE BIOSIS  
 ANSWER '20' FROM FILE BIOTECHDS  
 ANSWERS '21-25' FROM FILE SCISEARCH  
 ANSWERS '26-27' FROM FILE EMBASE

=> d iall 1-5; d ibib abs hitind 6-15; d ifull 16; d iall 17-27

L133 ANSWER 1 OF 27 MEDLINE on STN DUPLICATE 2  
 ACCESSION NUMBER: 2008688099 MEDLINE Full-text  
 DOCUMENT NUMBER: PubMed ID: 18790861  
 TITLE: RstA-promoted expression of the ferrous iron transporter  
 FeoB under iron-replete conditions enhances Fur activity in  
 Salmonella enterica.  
 AUTHOR: Jeon Jihye; Kim Hyunkeun; Yun Jiae; Ryu Sangryeol; Groisman  
 Eduardo A; Shin Dongwoo  
 CORPORATE SOURCE: Department of Molecular Cell Biology, Samsung Biomedical  
 Research Institute, Sungkyunkwan University School of  
 Medicine, Chunchun-dong 300, Jangan-gu, Suwon 440-746,  
 South Korea.  
 CONTRACT NUMBER: (United States Howard Hughes Medical Institute)  
 SOURCE: Journal of bacteriology, (2008 Nov) Vol. 190, No. 22, pp.  
 7326-34. Electronic Publication: 2008-09-12.  
 Journal code: 2985120R. E-ISSN: 1098-5530. L-ISSN:  
 0021-9193.  
 Report No.: NLM-PMC2576650.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200901  
 ENTRY DATE: Entered STN: 29 Oct 2008  
 Last Updated on STN: 14 Jan 2009  
 Entered Medline: 13 Jan 2009

#### ABSTRACT:

The Fur protein is a primary regulator that monitors and controls cytoplasmic iron levels. We now report the identification of a regulatory pathway mediated by the Salmonella response regulator RstA that promotes Fur activity. Genome-wide expression experiments revealed that under iron-replete conditions, expression of the RstA protein from a plasmid lowered transcription levels of various genes involved in iron acquisition. The RstA protein controlled iron-responsive genes through the Fur-Fe(II) protein because deletion of the \*\*\*fur\*\*\* gene or iron depletion abrogated RstA-mediated repression of these genes. The RstA protein maintained wild-type levels of the Fur protein but exceptionally activated transcription of the feoAB operon encoding the ferrous iron transporter FeoB by binding directly to the feoA promoter. This FeoB induction resulted in increased ferrous iron uptake, which associates with the Fur protein because lack of RstA-dependent transcriptional activation of the feoA promoter and feoB-deletion abolished repression of the Fur target genes by the RstA protein. Under iron-replete conditions, RstA expression retarded Salmonella growth but enabled the Fur protein to repress the target genes beyond the levels which were simply accomplished by iron.

CONTROLLED TERM: Bacterial Proteins: GE, genetics  
 \*Bacterial Proteins: ME, metabolism  
 Bacterial Proteins: PH, physiology  
 Blotting, Western  
 Electrophoretic Mobility Shift Assay

Gene Expression  
 Gene Expression Profiling  
 Gene Expression Regulation, Bacterial  
 Iron: DF, deficiency  
 \*Iron: ME, metabolism  
 Oligonucleotide Array Sequence Analysis  
 Operon: GE, genetics  
 Promoter Regions, Genetic: GE, genetics  
 Protein Binding  
 Repressor Proteins: GE, genetics  
 \*Repressor Proteins: ME, metabolism  
 Repressor Proteins: PH, physiology  
 Reverse Transcriptase Polymerase Chain Reaction  
   *Salmonella enterica*: GE, genetics  
   *Salmonella enterica*: GD, growth & development  
 \**Salmonella enterica*: ME, metabolism  
 Transcription, Genetic

CAS REGISTRY NO.: 7439-89-6 (Iron)

CHEMICAL NAME: 0 (Bacterial Proteins); 0 (Repressor Proteins); 0 (ferric uptake regulating proteins, bacterial)

MEDLINE REFERENCE COUNT: 35 There are 35 cited references available in MEDLINE for this document.

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L133 ANSWER 2 OF 27 MEDLINE on STN DUPLICATE 3  
 ACCESSION NUMBER: 2008507961 MEDLINE Full-text  
 DOCUMENT NUMBER: PubMed ID: 18656407  
 TITLE: Subinhibitory concentrations of tetracycline affect virulence gene expression in a multi-resistant Salmonella enterica subsp. enterica serovar Typhimurium DT104.  
 AUTHOR: Weir Emily K; Martin Laura C; Poppe Cornelis; Coombes Brian K; Boerlin Patrick  
 CORPORATE SOURCE: Laboratory for Foodborne Zoonoses, Public Health Agency of Canada, 110 Stone Road West, Guelph, Ontario, N1G 3W4, Canada.  
 SOURCE: Microbes and infection / Institut Pasteur, (2008 Jul) Vol. 10, No. 8, pp. 901-7. Electronic Publication: 2008-06-18. Journal code: 100883508. ISSN: 1286-4579. L-ISSN: 1286-4579.  
 PUB. COUNTRY: France  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200810  
 ENTRY DATE: Entered STN: 12 Aug 2008  
 Last Updated on STN: 22 Oct 2008  
 Entered Medline: 21 Oct 2008

## ABSTRACT:

Treatment of salmonellosis with antibiotics is controversial and may prolong carriage and shedding. Therefore, this study sought to investigate if exposure to antimicrobials influences the expression of factors involved in virulence and host colonization. The effect of subinhibitory tetracycline treatment (16 microg/ml, 30 min) on a multi-drug resistant Salmonella Typhimurium DT104 strain was investigated using a targeted microarray. Real-time reverse transcriptase PCR was used to confirm and further assess transcription of 10 selected genes. An in vitro cell invasion assay was performed to assess the invasiveness of the tetracycline-treated isolate. Out of 323 genes, 11 were significantly up-regulated and four were down-regulated in the microarray assays. The hild and hila genes, both regulators of Salmonella Pathogenicity Island 1, were up-regulated. Other up-regulated genes included the fliC, fliD, motA and motB genes, involved in motility, the fur gene, an important regulator of iron acquisition systems and of acid tolerance. The drug-exposed replicates showed a 2.5-fold increase in intracellular bacteria over the non-exposed control in cell cultures. These findings suggest a drug-induced expression profile consistent with the early stages of Salmonella infection and invasion concomitant with an increased ability to invade epithelial cells in vitro.

CONTROLLED TERM: \*Anti-Bacterial Agents: PD, pharmacology  
 Bacterial Proteins: BI, biosynthesis  
 Colony Count, Microbial  
 Cytoplasm: MI, microbiology  
 Drug Resistance, Multiple, Bacterial  
 Epithelial Cells: MI, microbiology  
 Gene Expression Profiling  
 \*Gene Expression Regulation, Bacterial: DE, drug effects  
 Hela Cells  
 Humans  
 Oligonucleotide Array Sequence Analysis  
 RNA, Bacterial: BI, biosynthesis

RNA, Messenger: BI, biosynthesis  
 Reverse Transcriptase Polymerase Chain Reaction  
 \*Salmonella typhimurium: DE, drug effects  
 \*Tetracycline: PD, pharmacology  
 Up-Regulation  
 \*Virulence Factors: BI, biosynthesis

CAS REGISTRY NO.: 60-54-8 (Tetracycline)  
 CHEMICAL NAME: 0 (Anti-Bacterial Agents); 0 (Bacterial Proteins); 0 (RNA, Bacterial); 0 (RNA, Messenger); 0 (Virulence Factors)

L133 ANSWER 3 OF 27 MEDLINE on STN DUPLICATE 4  
 ACCESSION NUMBER: 2007758095 MEDLINE Full-text  
 DOCUMENT NUMBER: PubMed ID: 18096019  
 TITLE: Expression of in vivo-inducible Salmonella enterica promoters during infection of Caenorhabditis elegans.  
 AUTHOR: Van Gerven Nani; Derous Veerle; Hernalsteens Jean-Pierre  
 SOURCE: FEMS microbiology letters, (2008 Jan) Vol. 278, No. 2, pp. 236-41.  
 Journal code: 7705721. ISSN: 0378-1097. L-ISSN: 0378-1097.  
 PUB. COUNTRY: England: United Kingdom  
 DOCUMENT TYPE: Letter  
 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200806  
 ENTRY DATE: Entered STN: 22 Dec 2007  
 Last Updated on STN: 3 Jun 2008  
 Entered Medline: 2 Jun 2008

## ABSTRACT:

In vitro mimicking of the stimuli controlling in vivo-inducible bacterial promoters during infection of the host can be complex. Therefore, the use of the nematode *Caenorhabditis elegans* was evaluated, as a surrogate host to examine the expression of *Salmonella enterica* promoters. Green fluorescent protein (GFP+) was put under the control of the promoters of the *pagC*, *mgtB*, *sseA*, *pgtE* and *fur* genes of *S. enterica*. After infection of *C. elegans* with an *S. enterica* serovar Typhimurium vaccine strain expressing these constructs, clear bacterial expression of GFP+ was observed under the control of all five promoters, although significant expression was not always obtained in vitro. It is concluded that *C. elegans* constitutes a useful model system for the study of the in vivo expression of *Salmonella* promoters.

CONTROLLED TERM: Adenosine Triphosphatases: GE, genetics  
 Animals  
 Bacterial Proteins: GE, genetics  
 \*Caenorhabditis elegans: MI, microbiology  
 Cation Transport Proteins: GE, genetics  
 Endopeptidases: GE, genetics  
 Gene Expression Regulation  
 Green Fluorescent Proteins: GE, genetics  
 Green Fluorescent Proteins: ME, metabolism  
 Membrane Proteins: GE, genetics  
 Microscopy, Fluorescence  
 Molecular Chaperones: GE, genetics  
 \*Promoter Regions, Genetic: GE, genetics  
 Repressor Proteins: GE, genetics  
 \*Salmonella enterica: GE, genetics  
 Salmonella enterica: GD, growth & development  
 Salmonella enterica: ME, metabolism

CAS REGISTRY NO.: 134773-72-1 (*pagC* protein, *Salmonella typhimurium*);  
 147336-22-9 (Green Fluorescent Proteins)  
 CHEMICAL NAME: 0 (Bacterial Proteins); 0 (Cation Transport Proteins); 0

(Membrane Proteins); 0 (Molecular Chaperones); 0 (Repressor Proteins); 0 (SseA protein, *Salmonella typhimurium*); 0 (ferric uptake regulating proteins, bacterial); EC 3.4.- (Endopeptidases); EC 3.4.- (PgtE protein, *Salmonella enterica*); EC 3.6.1.- (Adenosine Triphosphatases); EC 3.6.1.- (MgtB protein, *Salmonella typhimurium*)

L133 ANSWER 4 OF 27 MEDLINE on STN DUPLICATE 6  
 ACCESSION NUMBER: 1995238265 MEDLINE Full-text  
 DOCUMENT NUMBER: PubMed ID: 7536729  
 TITLE: The methylthio group (ms2) of N6-(4-hydroxyisopentenyl)-2-methylthioadenosine (ms2io6A) present next to the anticodon contributes to the decoding efficiency of the tRNA.  
 AUTHOR: Esberg B; Bjork G R  
 CORPORATE SOURCE: Department of Microbiology, Umea University, Sweden.  
 SOURCE: Journal of bacteriology, (1995 Apr) Vol. 177, No. 8, pp. 1967-75.  
 Journal code: 2985120R. ISSN: 0021-9193. L-ISSN: 0021-9193. Report No.: NLM-PMC176837.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199505  
 ENTRY DATE: Entered STN: 5 Jun 1995  
 Last Updated on STN: 29 Jan 1996  
 Entered Medline: 19 May 1995

## ABSTRACT:

A *Salmonella typhimurium* LT2 mutant which harbors a mutation (miaB2508::Tn10dCm) that results in a reduction in the activities of the amber suppressors supF30 (tRNA(CUATyr)), supD10 (tRNA(CUASer)), and supJ60 (tRNA(CUALeu)) was isolated. The mutant was deficient in the methylthio group (ms2) of N6-(4-hydroxyisopentenyl)-2-methylthioadenosine (ms2io6A), a modified nucleoside that is normally present next to the anticodon (position 37) in tRNAs that read codons that start with uridine. Consequently, the mutant had i6A37 instead of ms2io6A37 in its tRNA. Only small amounts of io6A37 was found. We suggest that the synthesis of ms2io6A occurs in the following order: A-37-->i6A37-->ms2i6A37-->ms2io6A37. The mutation miaB2508::Tn10dCm was 60% linked to the nag gene (min 15) and 40% linked to the fur

\*\*\*gene\*\*\* and is located counterclockwise from both of these genes. The growth rates of the mutant in four growth media did not significantly deviate from those of a wild-type strain. The polypeptide chain elongation rate was also unaffected in the mutant. However, the miaB2508::Tn10dCm mutation rendered the cell more resistant or sensitive, compared with a wild-type cell, to several amino acid analogs, suggesting that this mutation influences the regulation of several amino acid biosynthetic operons. The efficiencies of the aforementioned amber suppressors were decreased to as low as 16%, depending on the suppressor and the codon context monitored, demonstrating that the ms2 group of ms2io6A contributes to the decoding efficiency of tRNA. However, the major impact of the ms2io6 modification in the decoding process comes from the io6 group alone or from the combination of the ms2 and io6 groups, not from the ms2 group alone.

CONTROLLED TERM: \*Anticodon: CH, chemistry  
 \*Anticodon: GE, genetics  
 Base Sequence  
 Codon: GE, genetics  
 Genes, Bacterial  
 \*Isopentenyladenosine: AA, analogs & derivatives

Isopentenyladenosine: CH, chemistry  
 Molecular Sequence Data  
 Molecular Structure  
 Mutation  
 RNA, Bacterial: CH, chemistry  
 \*RNA, Bacterial: GE, genetics  
 \*RNA, Transfer, Amino Acid-Specific: CH, chemistry  
 \*RNA, Transfer, Amino Acid-Specific: GE, genetics  
   Salmonella typhimurium: GE, genetics  
   Salmonella typhimurium: GD, growth & development  
   Salmonella typhimurium: ME, metabolism  
 Suppression, Genetic

CAS REGISTRY NO.: 26190-61-4 (N(6)-(4-hydroxyisopentenyl)-2-methylthioadenosine); 7724-76-7 (Isopentenyladenosine)  
 CHEMICAL NAME: 0 (Anticodon); 0 (Codon); 0 (RNA, Bacterial); 0 (RNA, Transfer, Amino Acid-Specific)  
 GENE NAME: mia; nag  
 MEDLINE REFERENCE COUNT: 57      There are 57 cited references available in MEDLINE for this document.

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L133 ANSWER 5 OF 27 MEDLINE on STN DUPLICATE 7

ACCESSION NUMBER: 1994011346 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 8406841

TITLE: Role of acid tolerance response genes in Salmonella typhimurium virulence.

AUTHOR: Garcia-del Portillo F; Foster J W; Finlay B B

CORPORATE SOURCE: Biotechnology Laboratory, University of British Columbia, Vancouver, Canada.

SOURCE: Infection and immunity, (1993 Oct) Vol. 61, No. 10, pp. 4489-92.  
Journal code: 0246127. ISSN: 0019-9567. L-ISSN: 0019-9567.  
Report No.: NLM-PMC281185.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199311

ENTRY DATE: Entered STN: 17 Jan 1994  
Last Updated on STN: 3 Feb 1997  
Entered Medline: 16 Nov 1993

## ABSTRACT:

The *atp* and *fur* genes are involved in the acid tolerance response of *Salmonella typhimurium*. An *atp::Tn10* mutant was avirulent in the mouse typhoid model when assayed by oral and intraperitoneal routes. However, a *fur* mutant was completely virulent by the intraperitoneal route. No relevant differences in intracellular survival or invasion rates were observed for the two mutants in macrophages and epithelial cells. These data indicate that separate acid tolerance response genes may have different roles in *S. typhimurium* virulence.

CONTROLLED TERM: Animals  
\*Bacterial Proteins: ME, metabolism  
Dogs  
\*Genes, Bacterial  
Hela Cells  
Humans  
Hydrogen-Ion Concentration  
Mice

Mice, Inbred BALB C  
 Mutagenesis, Insertional  
 \*Proton-Translocating ATPases: ME, metabolism  
 \*Repressor Proteins: ME, metabolism  
     *Salmonella typhimurium*: GE, genetics  
     \**Salmonella typhimurium*: FY, pathogenicity  
     Typhoid Fever: MI, microbiology  
 CHEMICAL NAME: 0 (Bacterial Proteins); 0 (Repressor Proteins); 0 (ferric uptake regulating proteins, bacterial); EC 3.6.3.14 (Proton-Translocating ATPases)  
 GENE NAME: atp; fur; unc  
 MEDLINE REFERENCE COUNT: 23 There are 23 cited references available in MEDLINE for this document.

REFERENCE(S): CITED REFERENCES AVAILABLE IN MEDLINE

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- (22) Buchmeier, N A; Infect Immun. 1989 Jan, V57(1), P1-7. MEDLINE
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L133 ANSWER 6 OF 27 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2010:1221418 CAPLUS Full-text  
 DOCUMENT NUMBER: 153:478805  
 TITLE: Recombinant *Salmonella enterica* strains presenting  
         Campylobacter jejuni N-glycan  
 INVENTOR(S): Ilg, Karin; Aebi, Markus; Ahuja, Umesh; Amber, Saba;  
               Schwarz, Flavio  
 PATENT ASSIGNEE(S): Eidgenoessische Technische Hochschule Zuerich, Switz.  
 SOURCE: PCT Int. Appl., 39pp.  
         CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2010108682      A1      20100930      WO 2010-EP1884      20100325
W:  AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,
    CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG,
    ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP,
    KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA,
    MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE,
    PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV,
    SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,
    IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI,
    SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
    SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ,
    UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

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PRIORITY APPLN. INFO.:

EP 2009-4445

A 20090327

AB The present invention relates to *Salmonella enterica* comprising at least one *pgl* operon of *Campylobacter jejuni* or a functional derivative thereof and presenting at least one N- glycan of *Campylobacter jejuni* or N-glycan derivative thereof on its cell surface. In addition, it is directed to medical uses and pharmaceutical compns. thereof as well as methods for treating and/or preventing *Campylobacter* and optionally *Salmonella* infections and methods for producing these *Salmonella* strains. IPCI C12N0001-20 [I,A]; C12N0001-36 [I,A]; C07K0014-205 [I,A]; C07K0014-195

[I,C\*]; A61K0039-106 [I,A]

IPCR C12N0001-20 [I,C]; C12N0001-20 [I,A]; A61K0039-106 [I,C]; A61K0039-106 [I,A]; C07K0014-195 [I,C]; C07K0014-205 [I,A]; C12N0001-36 [I,C]; C12N0001-36 [I,A]

CC 16-2 (Fermentation and Bioindustrial Chemistry)

Section cross-reference(s): 3, 10

IT Gene, microbial

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(aro, claimed *Salmonella* gene mutated for attenuation;  
recombinant *Salmonella enterica* strains presenting *Campylobacter jejuni* N-glycan)

IT Gene, microbial

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(aroA, claimed *Salmonella* gene mutated for attenuation;  
recombinant *Salmonella enterica* strains presenting *Campylobacter jejuni* N-glycan)

IT Gene, microbial

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(asd, claimed *Salmonella* gene mutated for attenuation;  
recombinant *Salmonella enterica* strains presenting *Campylobacter jejuni* N-glycan)

IT Gene, microbial

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(cdt, claimed *Salmonella* gene mutated for attenuation;  
recombinant *Salmonella enterica* strains presenting *Campylobacter jejuni* N-glycan)

IT Gene, microbial

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(crp, claimed *Salmonella* gene mutated for attenuation;  
recombinant *Salmonella enterica* strains presenting *Campylobacter jejuni* N-glycan)

IT Gene, microbial

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(cya, claimed *Salmonella* gene mutated for attenuation;  
recombinant *Salmonella enterica* strains presenting *Campylobacter jejuni* N-glycan)

IT Gene, microbial

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (dap, claimed Salmonella gene mutated for attenuation;  
 recombinant Salmonella enterica strains presenting Campylobacter jejuni  
 N-glycan)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (fur, claimed Salmonella gene mutated for  
 attenuation; recombinant Salmonella enterica strains presenting  
 Campylobacter jejuni N-glycan)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (galE, claimed Salmonella gene mutated for attenuation;  
 recombinant Salmonella enterica strains presenting Campylobacter jejuni  
 N-glycan)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (galU, claimed Salmonella gene mutated for attenuation;  
 recombinant Salmonella enterica strains presenting Campylobacter jejuni  
 N-glycan)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (hemA, claimed Salmonella gene mutated for attenuation;  
 recombinant Salmonella enterica strains presenting Campylobacter jejuni  
 N-glycan)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (htrA, claimed Salmonella gene mutated for attenuation;  
 recombinant Salmonella enterica strains presenting Campylobacter jejuni  
 N-glycan)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (nadA, claimed Salmonella gene mutated for attenuation;  
 recombinant Salmonella enterica strains presenting Campylobacter jejuni  
 N-glycan)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (ompR, claimed Salmonella gene mutated for attenuation;  
 recombinant Salmonella enterica strains presenting Campylobacter jejuni  
 N-glycan)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (pab, claimed Salmonella gene mutated for attenuation;  
 recombinant Salmonella enterica strains presenting Campylobacter jejuni  
 N-glycan)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (phoP, claimed Salmonella gene mutated for attenuation;  
 recombinant Salmonella enterica strains presenting Campylobacter jejuni  
 N-glycan)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (phoQ, claimed Salmonella gene mutated for attenuation;  
 recombinant Salmonella enterica strains presenting Campylobacter jejuni  
 N-glycan)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (pmi, claimed Salmonella gene mutated for attenuation;  
 recombinant Salmonella enterica strains presenting Campylobacter jejuni  
 N-glycan)

IT Gene, microbial

- RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (pncB, claimed Salmonella gene mutated for attenuation;  
 recombinant Salmonella enterica strains presenting Campylobacter jejuni  
 N-glycan)
- IT Gene, microbial  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (poxA, claimed Salmonella gene mutated for attenuation;  
 recombinant Salmonella enterica strains presenting Campylobacter jejuni  
 N-glycan)
- IT Gene, microbial  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (pur, claimed Salmonella gene mutated for attenuation;  
 recombinant Salmonella enterica strains presenting Campylobacter jejuni  
 N-glycan)
- IT Bos taurus  
 Cattle  
 DNA sequences  
 Feed additives  
 Food additives  
 Genetic engineering  
 Immunization  
 Livestock  
 Mouse  
 Mus musculus  
 Plasmid vectors  
 Poultry  
 Protein sequences  
 Salmonella enterica  
 Salmonella enterica enterica gallinarum  
 Salmonella enteritidis  
 Salmonella hadar  
 Salmonella heidelberg  
 Salmonella infantis  
 Salmonella kentucky  
 Salmonella typhimurium  
 Vaccines  
 (recombinant Salmonella enterica strains presenting Campylobacter  
 jejuni N-glycan)
- IT Glycoconjugates  
 Lipid A  
 O antigen  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (recombinant Salmonella enterica strains presenting Campylobacter  
 jejuni N-glycan)
- IT Gene, microbial  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (rfc, claimed Salmonella gene mutated for attenuation;  
 recombinant Salmonella enterica strains presenting Campylobacter jejuni  
 N-glycan)

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L133 ANSWER 7 OF 27 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:694425 CAPLUS Full-text

DOCUMENT NUMBER: 151:73220

TITLE: O-antigen-negative Salmonella enterica serovar  
 typhimurium is attenuated in intestinal  
 colonization but elicits colitis in  
 streptomycin-treated mice

AUTHOR(S): Ilg, Karin; Endt, Kathrin; Misselwitz, Benjamin;

CORPORATE SOURCE: Stecher, Barbel; Aebi, Markus; Hardt, Wolf-Dietrich  
 Institut fur Mikrobiologie, Eidgenossische Technische  
 Hochschule, ETH Zurich, Zurich, CH-8093, Switz.

SOURCE: Infection and Immunity (2009), 77(6), 2568-2575  
 CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Lipopolysaccharide (LPS) is a major constituent of the outer membrane and an important virulence factor of *Salmonella enterica* subspecies 1 serovar Typhimurium (serovar Typhimurium). To evaluate the role of LPS in eliciting intestinal inflammation in streptomycin-treated mice, we constructed an O-antigen-deficient serovar Typhimurium strain through deletion of the *wbaP* gene. The resulting strain was highly susceptible to human complement activity and the antimicrobial peptide mimic polymyxin B. Furthermore, it showed a severe defect in motility and an attenuated phenotype in a competitive mouse infection experiment, where the  $\Delta wbaP$  strain (SKI12) was directly compared to wild-type *Salmonella*. Nevertheless, the  $\Delta wbaP$  strain (SKI12) efficiently invaded HeLa cells in vitro and elicited acute intestinal inflammation in streptomycin-pretreated mice. These expts. prove that the presence of complete LPS is not essential for in vitro invasion or for triggering acute colitis.

CC 10-6 (Microbial, Algal, and Fungal Biochemistry)  
 Section cross-reference(s): 1, 13

IT Colitis  
 Intestine  
 Mouse  
*Mus musculus*  
*Salmonella typhimurium*  
 (O-antigen-neg. *Salmonella typhimurium* is attenuated in intestinal colonization but elicits colitis in streptomycin-treated mice)

IT Lipopolysaccharides  
 O antigen  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (O-antigen-neg. *Salmonella typhimurium* is attenuated in intestinal colonization but elicits colitis in streptomycin-treated mice)

IT 57-92-1, Streptomycin  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (O-antigen-neg. *Salmonella typhimurium* is attenuated in intestinal colonization but elicits colitis in streptomycin-treated mice)

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD  
 (4 CITINGS)

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L133 ANSWER 8 OF 27 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2007:357849 CAPLUS Full-text

DOCUMENT NUMBER: 146:336130

TITLE: Intranasal immunization with heterologously expressed polysaccharide protects against multiple *Pseudomonas aeruginosa* infections

AUTHOR(S): DiGiandomenico, Antonio; Rao, Jayasimha; Harcher, Katie; Zaidi, Tanweer S.; Gardner, Jason; Neely, Alice N.; Pier, Gerald B.; Goldberg, Joanna B.

CORPORATE SOURCE: Dep. Microbiol., Univ. Virginia Health System,  
 Charlottesville, VA, 22908, USA

SOURCE: Proceedings of the National Academy of Sciences of the

United States of America (2007), 104(11), 4624-4629

CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Surface-expressed bacterial polysaccharides are often immunodominant, protective antigens. However, these antigens are chemical and serol. highly heterogeneous, and conjugation to protein carriers is often necessary to enhance their immunogenicity. Here the authors show the efficacy of intranasal immunization of mice with attenuated *Salmonella enterica* typhimurium expressing the O antigen portion of *P. aeruginosa* lipopolysaccharide. *P. aeruginosa* is an ideal model system because it can cause a myriad of localized and systemic infections. In particular, this bacterium is a leading cause of hospital-acquired pneumonia and is responsible for infections after burns and after eye injury. In addition, there are mouse models of infection that mimic the clin. manifestations of *P. aeruginosa* infections. Immunized mice were highly protected against infection, with long-lasting immunity to acute *P. aeruginosa* pneumonia, whereas mice immunized with *Salmonella* containing only the cloning vector or PBS were not. Prophylactic and therapeutic administration of sera from vaccinated animals protected naive mice. Intranasal vaccination also provided complete protection from infections after burns and reduced pathol. after corneal abrasions. Thus, intranasal delivery of heterologously expressed polysaccharide antigens provides protection at distinct sites of infection. This approach for the expression and delivery of polysaccharide antigens as recombinant immunogens could be easily adapted to develop vaccines for many infectious agents, without the need for complicated purification and conjugation procedures.

CC 15-2 (Immunochemistry)

IT Lipopolysaccharides

RL: BSU (Biological study, unclassified); BIOL (Biological study) (bacterial; heterologous expression of *Pseudomonas aeruginosa* lipopolysaccharide O antigen in attenuated *Salmonella* vector as intranasal vaccine)

IT *Pseudomonas aeruginosa**Salmonella enterica* typhimurium

(heterologous expression of *Pseudomonas aeruginosa* lipopolysaccharide O antigen in attenuated *Salmonella* vector as intranasal vaccine)

IT O antigen

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(heterologous expression of *Pseudomonas aeruginosa* lipopolysaccharide O antigen in attenuated *Salmonella* vector as intranasal vaccine)

IT Vaccines

(nasal; heterologous expression of *Pseudomonas aeruginosa* lipopolysaccharide O antigen in attenuated *Salmonella* vector as intranasal vaccine)

IT Antigens

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(protective; heterologous expression of *Pseudomonas aeruginosa* lipopolysaccharide O antigen in attenuated *Salmonella* vector as intranasal vaccine)

OS.CITING REF COUNT: 19 THERE ARE 19 CAPLUS RECORDS THAT CITE THIS RECORD (19 CITINGS)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L133 ANSWER 9 OF 27 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2006:1056021 CAPLUS Full-text

DOCUMENT NUMBER: 145:354218

TITLE: Down-regulation of key virulence factors makes the *Salmonella enterica* serovar Typhimurium rfaH mutant a promising live-attenuated vaccine candidate

AUTHOR(S): Nagy, Gabor; Danino, Vittoria; Dobrindt, Ulrich; Pallen, Mark; Chaudhuri, Roy; Emody, Levente; Hinton, Jay C.; Hacker, Jorg

CORPORATE SOURCE: Department of Medical Microbiology and Immunology, University of Pecs, Pecs, 7624, Hung.

SOURCE: Infection and Immunity (2006), 74(10), 5914-5925  
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Mutants of *Salmonella enterica* serovar Typhimurium that lack the transcriptional regulator RfaH are efficient as live oral vaccines against salmonellosis in mice. The authors show that the attenuation of the vaccine candidate strain is associated with reduced net growth in epithelial and macrophage cells. To identify the relevant RfaH-dependent genes, the RfaH regulon was determined with *S. enterica* serovars Enteritidis and Typhimurium using whole-genome *Salmonella* microarrays. As well as impacting the expression of genes involved in lipopolysaccharide (LPS) core and O-antigen synthesis, the loss of RfaH results in a marked down-regulation of SPI-4 genes, the flagellum/chemotaxis system, and type III secretion system 1. However, a proportion of these effects could have been the indirect consequence of the altered expression of genes required for LPS biosynthesis. Direct and indirect effects of the rfaH mutation were dissociated by genome-wide transcriptional profiling of a structural deep-rough LPS mutant (waaG). The authors show that truncation of LPS itself is responsible for the decreased intracellular yield observed for  $\Delta$ rfaH strains. LPS mutants do not differ in replication ability; rather, they show increased susceptibility to antimicrobial peptides in the intracellular milieu. Evidence that deletion of rfaH, as well as some other genes involved in LPS biosynthesis, results in enhanced invasion of various mammalian cells is shown. Exposure of common minor antigens in the absence of serovar-specific antigens might be responsible for the observed cross-reactive nature of the elicited immune response upon vaccination. Increased invasiveness of the *Salmonella* rfaH mutant into antigen-presenting cells, combined with increased intracellular killing and the potential for raising a cross-protective immune response, renders the rfaH mutant an ideal vaccine candidate.

CC 15-2 (Immunochemistry)

IT Gene, microbial

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(SPI-4; down-regulation of key virulence factors makes the *Salmonella enterica* serovar Typhimurium rfaH mutant a promising live-attenuated vaccine candidate)

IT Lipopolysaccharides

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(bacterial; down-regulation of key virulence factors makes the *Salmonella enterica* serovar Typhimurium rfaH mutant a promising live-attenuated vaccine candidate)

IT Antigen-presenting cell

Epithelium

Gene expression profiles, microbial

Macrophage

Regulon

*Salmonella enterica* typhimurium

Vaccines

Virulence (microbial)  
 (down-regulation of key virulence factors makes the *Salmonella enterica* serovar Typhimurium rfaH mutant a promising live-attenuated vaccine candidate)

## IT O antigen

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (down-regulation of key virulence factors makes the *Salmonella enterica* serovar Typhimurium rfaH mutant a promising live-attenuated vaccine candidate)

## IT Antimicrobial agents

(peptide; down-regulation of key virulence factors makes the *Salmonella enterica* serovar Typhimurium rfaH mutant a promising live-attenuated vaccine candidate)

## IT Transcription factors

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (rfaH; down-regulation of key virulence factors makes the *Salmonella enterica* serovar Typhimurium rfaH mutant a promising live-attenuated vaccine candidate)

## IT Gene, microbial

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (waaG; down-regulation of key virulence factors makes the *Salmonella enterica* serovar Typhimurium rfaH mutant a promising live-attenuated vaccine candidate)

## IT Gene, microbial

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (waaL; down-regulation of key virulence factors makes the *Salmonella enterica* serovar Typhimurium rfaH mutant a promising live-attenuated vaccine candidate)

## IT Gene, microbial

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (waaP; down-regulation of key virulence factors makes the *Salmonella enterica* serovar Typhimurium rfaH mutant a promising live-attenuated vaccine candidate)

## IT Gene, microbial

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (waaY; down-regulation of key virulence factors makes the *Salmonella enterica* serovar Typhimurium rfaH mutant a promising live-attenuated vaccine candidate)

## IT 1404-26-8, Polymyxin B

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (down-regulation of key virulence factors makes the *Salmonella enterica* serovar Typhimurium rfaH mutant a promising live-attenuated vaccine candidate)

OS.CITING REF COUNT: 24 THERE ARE 24 CAPLUS RECORDS THAT CITE THIS RECORD (24 CITINGS)

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L133 ANSWER 10 OF 27 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2007:1066806 CAPLUS Full-text

DOCUMENT NUMBER: 148:353607

TITLE: Synthesis and immunogenicity in mice of conjugate vaccine of *Salmonella paratyphi* A O-SP bound to tetanus toxoid

AUTHOR(S): Zhao, Zhi-qiang; Yang, Zhao-hui; Ji, Yong-li; Du, Lin; Xie, Gui-lin

CORPORATE SOURCE: Lanzhou Institute of Biological Products, Lanzhou, 730046, Peop. Rep. China

SOURCE: Zhonghua Weishengwuxue He Mianyixue Zazhi (2006),

26(11), 1048-1052  
 CODEN: ZWMZDP; ISSN: 0254-5101  
 Beijing Shengwu Zhipin Yanjiuso

PUBLISHER:  
 DOCUMENT TYPE:  
 LANGUAGE:

Chinese

AB The objective is to develop polysaccharide-protein conjugate vaccine for preventing *Salmonella paratyphi* A infection. *Salmonella paratyphi* A NTP-6 strain was fermented, then LPS was extracted with hot-Ph method and detoxified with 1% acetic acid at 100 °C for 1.5 h; the O-SP mixture was purified with Sephadex G-75, and the first and second peak were collected as effective polysaccharide antigen. O-SP was activated with CDAP, bound to TT with ADH as a spacer, and condensed with EDAC. Solns. of 2.5 µg of saccharide, alone or as conjugate, were injected s.c. into young mice. Antibodies against LPS in serum of the mice were measured by ELISA. Complement-mediated bactericidal activity was also assayed. The safety of conjugate vaccine was evaluated in mice and guinea pig. After the second injection, the mean geometric titer (GMT) of anti-LPS IgG increased by more than 4 times, and the third injection showed significantly booster response. In the complement-mediated bactericidal activity test, the titers of antiserum were above 1:1280. In mice and guinea pig, conjugate vaccine had not shown any harmful effect. A *Salmonella paratyphi* A conjugate vaccine preparation procedure was successfully constructed. The TI antigen of O-SP was effectively converted into TD antigen; clin. evaluation of *S. paratyphi* A conjugate vaccine is planned.

CC 15-10 (Immunochemistry)

IT Antigens

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (polysaccharide; synthesis and immunogenicity in mice of conjugate vaccine of *Salmonella paratyphi* A O-SP bound to tetanus toxoid)

IT Blood serum

Immunity

*Salmonella paratyphi*-A

Vaccines

(synthesis and immunogenicity in mice of conjugate vaccine of *Salmonella paratyphi* A O-SP bound to tetanus toxoid)

IT Lipopolysaccharides

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (synthesis and immunogenicity in mice of conjugate vaccine of *Salmonella paratyphi* A O-SP bound to tetanus toxoid)

L133 ANSWER 11 OF 27 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2005:1289148 CAPLUS Full-text

DOCUMENT NUMBER: 144:35285

TITLE: Live, oral vaccine for protection against *Shigella dysenteriae* serotype 1

INVENTOR(S): Kopecko, Dennis J.; Xu, Deqi

PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA

SOURCE: PCT Int. Appl., 55 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005116063	A1	20051208	WO 2005-US18198	20050524
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,				



GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,  
 LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,  
 NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,  
 SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,  
 ZA, ZM, ZW  
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,  
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,  
 EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,  
 RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,  
 MR, NE, SN, TD, TG  
 EP 1756149 A1 20070228 EP 2005-754091 20050524  
 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,  
 IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR  
 US 20080193486 A1 20080814 US 2007-597301 20070921  
 PRIORITY APPLN. INFO.: US 2004-574279P P 20040524  
 US 2004-609494P P 20040913  
 WO 2005-US18198 W 20050524

AB The authors disclose the mol. cloning and functional characterization of the  
 rfb locus and rfp plasmid gene of *Shigella dysenteriae*. The products of the genes  
 are shown to be sufficient for the biosynthesis core-linked O-specific  
 polysaccharide in bacterial vectors. When expressed in vaccine delivery systems,  
 the O-specific polysaccharide may provide protective immunity against shigellosis.  
 IPCI C07K0014-25 [ICM,7]; C07K0014-195 [ICM,7,C\*]; A61K0039-112 [ICS,7]  
 IPCR C07K0014-195 [I,C\*]; C07K0014-25 [I,A]; C12N0015-52 [I,C\*]; C12N0015-52  
 [I,A]  
 CC 15-2 (Immunochemistry)  
 Section cross-reference(s): 3, 7, 10, 14  
 IT Dysentery  
 Human  
 Prophylaxis  
 Salmonella typhi  
 Shigella dysenteriae  
 (Shigella dysenteriae O-polysaccharide biosynthetic enzymes expressed  
 in bacterial vectors as oral vaccine against dysentery)  
 IT O antigen  
 RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL  
 (Biological study); PREP (Preparation); USES (Uses)  
 (Shigella dysenteriae O-polysaccharide biosynthetic enzymes  
 expressed in bacterial vectors as oral vaccine against dysentery)  
 IT Lipopolysaccharides  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (bacterial; cloning of Shigella dysenteriae biosynthetic enzymes for  
 O-antigenic polysaccharide of)  
 IT Plasmid vectors  
 (for expression of Shigella dysenteriae O-polysaccharide biosynthetic  
 enzymes in attenuated bacteria)  
 IT Promoter (genetic element)  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (of rfb locus for expression of Shigella dysenteriae O-polysaccharide  
 biosynthetic enzymes in attenuated bacteria)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L133 ANSWER 12 OF 27 CAPLUS COPYRIGHT 2010 ACS on STN  
 ACCESSION NUMBER: 1999:8105 CAPLUS Full-text  
 DOCUMENT NUMBER: 130:71518  
 TITLE: Live attenuated bacterial vaccines  
 containing a modified iron uptake fur  
 gene  
 INVENTOR(S): Baldwin, Thomas John; Borriello, Saverio Peter;

PATENT ASSIGNEE(S): Palmer, Helen Mary  
 SOURCE: Medical Research Council, UK  
 PCT Int. Appl., 49 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9856901	A2	19981217	WO 1998-GB1683	19980609
WO 9856901	A3	19990318		
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
CA 2292900	A1	19981217	CA 1998-2292900	19980609
AU 9880268	A	19981230	AU 1998-80268	19980609
AU 745003	B2	20020307		
EP 996712	A2	20000503	EP 1998-928436	19980609
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
BR 9809974	A	20010918	BR 1998-9974	19980609
JP 2002511752	T	20020416	JP 1999-501891	19980609
PRIORITY APPLN. INFO.:			GB 1997-11964	A 19970609
			WO 1998-GB1683	W 19980609

AB An attenuated bacterium in which the native *fur* gene, or homolog thereof, is modified such that the expression of the *fur* gene product, or homolog thereof, is regulated independently of the iron concentration in the environment of the bacterium, is suitable for use as a live vaccine. This has important implications in the manufacture of live vaccines since the increased expression of the protective antigens during the manufacture process will increase the efficacy of the live vaccine when administered to an animal or human subject. For alterations in the *fur* gene it is essential not to have a complete knockout mutant since this may be lethal. Thus, the *fur* gene may be placed under the control of another promoter which can be switched on or off independently of the factors (iron) which normally controls *fur* expression. Preferably, the bacterium is also attenuated by mutation of at least one gene essential for the production of a metabolite or catabolite not produced by a human or animal; such mutations may be in an *aro* gene such as an *aroB* gene and/or *aroL* gene and/or a gene of the *pur* or *pyr* pathways. The bacterium may be, in particular, *Neisseria meningitidis*. IPCI C12N0015-00 [ICM,6]

IPCR C12N0015-09 [I,C\*]; C12N0015-09 [I,A]; A61K0039-00 [N,C\*]; A61K0039-00 [N,A]; A61K0039-095 [I,C\*]; A61K0039-095 [I,A]; A61K0039-10 [I,C\*]; A61K0039-10 [I,A]; A61K0039-102 [I,C\*]; A61K0039-102 [I,A]; A61K0039-104 [I,C\*]; A61K0039-104 [I,A]; A61K0039-108 [I,C\*]; A61K0039-108 [I,A]; A61K0039-112 [I,C\*]; A61K0039-112 [I,A]; A61P0031-00 [I,C\*]; A61P0031-04 [I,A]; C07K0014-195 [I,C\*]; C07K0014-22 [I,A]; C12N0001-20 [I,C\*]; C12N0001-20 [I,A]; C12N0001-21 [I,C\*]; C12N0001-21 [I,A]; C12R0001-36 [N,A]

CC 63-3 (Pharmaceuticals)

Section cross-reference(s): 3, 10

ST bacteria vaccine attenuation *fur* gene;  
*Neisseria* vaccine attenuation *fur* gene

IT Transcription factors

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (Fur (ferric uptake regulation), mutation of gene  
 fur for; live attenuated bacterial vaccines containing a  
 modified iron uptake fur gene)

IT Proteins, specific or class  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (Op (opacity protein), mutation of gene opc for; live  
 attenuated bacterial vaccines containing a modified iron uptake  
 fur gene)

IT Gene, microbial  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (aro; live attenuated bacterial vaccines containing a modified  
 iron uptake fur gene)

IT Gene, microbial  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (aroB; live attenuated bacterial vaccines containing a modified  
 iron uptake fur gene)

IT Gene, microbial  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (aroL; live attenuated bacterial vaccines containing a modified  
 iron uptake fur gene)

IT Gene, microbial  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (asd; live attenuated bacterial vaccines containing a modified  
 iron uptake fur gene)

IT Mutagenesis  
 (attenuating; live attenuated bacterial vaccines  
 containing a modified iron uptake fur gene)

IT Gene, microbial  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (comA; live attenuated bacterial vaccines containing a modified  
 iron uptake fur gene)

IT Gene, microbial  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (fur; live attenuated bacterial vaccines containing a  
 modified iron uptake fur gene)

IT Gene, microbial  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (gale; live attenuated bacterial vaccines containing a modified  
 iron uptake fur gene)

IT Enzymes, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (gene recA, mutation of gene recA for; live  
 attenuated bacterial vaccines containing a modified iron uptake  
 fur gene)

IT Bacteria (Eubacteria)  
 Bordetella pertussis  
 Escherichia coli  
 Gram-negative bacteria  
 Haemophilus influenzae  
 Helicobacter pylori  
 Neisseria gonorrhoeae  
 Neisseria meningitidis  
 Pseudomonas aeruginosa  
 Salmonella typhi  
 Salmonella typhimurium  
 Shigella  
 Vibrio cholerae  
 (live attenuated bacterial vaccines containing a modified iron  
 uptake fur gene)

IT Gene, microbial  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (minB; live attenuated bacterial vaccines containing a modified  
 iron uptake fur gene)

IT Gene, microbial  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (opc; live attenuated bacterial vaccines containing a modified  
 iron uptake fur gene)

IT Gene, microbial  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (pur; live attenuated bacterial vaccines containing a modified  
 iron uptake fur gene)

IT Gene, microbial  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (purB; live attenuated bacterial vaccines containing a modified  
 iron uptake fur gene)

IT Gene, microbial  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (purE; live attenuated bacterial vaccines containing a modified  
 iron uptake fur gene)

IT Gene, microbial  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (pyr; live attenuated bacterial vaccines containing a modified  
 iron uptake fur gene)

IT Gene, microbial  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (pyrA; live attenuated bacterial vaccines containing a modified  
 iron uptake fur gene)

IT Gene, microbial  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (pyrB; live attenuated bacterial vaccines containing a modified  
 iron uptake fur gene)

IT Gene, microbial  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (recA; live attenuated bacterial vaccines containing a modified  
 iron uptake fur gene)

IT Vaccines  
 (synthetic; live attenuated bacterial vaccines containing a  
 modified iron uptake fur gene)

IT 37211-77-1, 3-Dehydroquinate synthase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (mutation of gene aroB for; live attenuated  
 bacterial vaccines containing a modified iron uptake fur  
 gene)

IT 9031-51-0, Shikimate kinase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (mutation of gene aroL for; live attenuated  
 bacterial vaccines containing a modified iron uptake fur  
 gene)

IT 9000-98-0, Aspartate semialdehyde dehydrogenase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (mutation of gene asd for; live attenuated  
 bacterial vaccines containing a modified iron uptake fur  
 gene)

IT 9032-89-7, UDP-galactose 4-epimerase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (mutation of gene gale for; live attenuated  
 bacterial vaccines containing a modified iron uptake fur  
 gene)

IT 9027-81-0, Adenylosuccinate lyase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (mutation of gene purB for; live attenuated  
 bacterial vaccines containing a modified iron uptake fur  
 gene)

IT 9032-04-6, Phosphoribosylaminoimidazole carboxylase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (mutation of gene purE for; live attenuated  
 bacterial vaccines containing a modified iron uptake fur  
 gene)

IT 9026-23-7, Carbamyl phosphate synthetase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (mutation of gene pyrA for; live attenuated  
 bacterial vaccines containing a modified iron uptake fur  
 gene)

IT 9012-49-1, Aspartate transcarbamylase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (mutation of gene pyrB for; live attenuated  
 bacterial vaccines containing a modified iron uptake fur  
 gene)

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD  
 (6 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L133 ANSWER 13 OF 27 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1993:140868 CAPLUS Full-text

DOCUMENT NUMBER: 118:140868

ORIGINAL REFERENCE NO.: 118:24095a,24098a

TITLE: Molecular cloning and characterization of the genetic  
 determinants that express the complete Shigella  
 serotype D (Shigella sonnei) lipopolysaccharide in  
 heterologous live attenuated vaccine strains

AUTHOR(S): Viret, Jean Francois; Cryz, Stanley J., Jr.; Lang,  
 Alois B.; Favre, Didier

CORPORATE SOURCE: Swiss Serum Vaccine Inst., Bern, CH-3018, Switz.

SOURCE: Molecular Microbiology (1993), 7(2), 239-52

CODEN: MOMIEE; ISSN: 0950-382X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The genetic determinants for the complete S. sonnei lipopolysaccharide (LPS)  
 were cloned, characterized by restriction mapping, and expressed in  
 heterologous genetic backgrounds, including Salmonella typhi and Vibrio  
 cholerae live attenuated vaccine strains. The rfb/rfc locus encoding the  
 polymerized serotype-specific O polysaccharide was mapped within 23 kb of DNA  
 isolated from S. sonnei virulence plasmid pWR105. A highly similar  
 chromosomal DNA sequence was identified by Southern hybridization anal. in  
 Plesiomonas shigelloides known to have the same O serotype specificity as S.  
 sonnei. Expression studies of the rfb/rfc locus have shown that S. sonnei O  
 polysaccharide is covalently bound to LPS cores of both the K-12 and R1 types,  
 but neither to Salmonella (Ra-type) nor to V. cholerae O1 cores. In order to  
 express a compatible core structure in the latter organisms, chromosomal rfa  
 loci encoding R1-type LPS were isolated from both an Escherichia coli R1  
 strain (rfaR1) and from S. sonnei (rfasonnei). Restriction mapping and  
 functional anal. of cloned DNA allowed localization of the rfaR1 locus and its  
 orientation with respect to the neighboring cysE chromosomal marker. A high  
 degree of sequence similarity was found at the DNA level between rfa loci of  
 enterobacterial species characterized by R1-type LPS. Co-expression studies  
 involving S. sonnei rfb/rfc and rfa loci propagated on compatible plasmids  
 have shown that, at most, 13 to 14 kb of rfaR1 DNA are required for the  
 expression of complete phase-I-like S. sonnei LPS in E. coli K-12 and S.

typhi, whereas an adjacent region of about 3.5 kb is needed in the more stringent host, *V. cholerae*. *S. sonnei* O antigen expressed in a *V. cholerae* recombinant vaccine strain is present on the cell surface in a form suitable for the induction of a specific antibody response in vaccinated rabbits.

CC 3-2 (Biochemical Genetics)  
 Section cross-reference(s): 15, 63  
 IT Lipopolysaccharides  
 RL: BIOL (Biological study)  
 (genes for, of *Shigella sonnei* serotype D, cloning and mapping of)  
 IT *Salmonella typhi*  
*Vibrio cholerae*  
 (lipopolysaccharide genes of *Shigella sonnei* serotype D cloning and expression in live attenuated vaccine strains of)  
 IT Molecular cloning  
 (of lipopolysaccharide genes, of *Shigella sonnei* serotype D, in live attenuated oral vaccine strains)  
 IT Antigens  
 RL: BIOL (Biological study)  
 (O, genes for, of *Shigella sonnei*, mapping and expression in live attenuated vaccine strains of)  
 OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)

L133 ANSWER 14 OF 27 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1988:427599 CAPLUS Full-text  
 DOCUMENT NUMBER: 109:27599  
 ORIGINAL REFERENCE NO.: 109:4621a,4624a  
 TITLE: Preparation and use of recombinant avirulent  
*Salmonella* strains as vaccines against cholera  
 INVENTOR(S): Morona, Renato  
 PATENT ASSIGNEE(S): Enterovax Research Pty. Ltd., Australia  
 SOURCE: Eur. Pat. Appl., 14 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
EP 257837	A1	19880302	EP 1987-306833	19870731
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AU 8776269	A	19880225	AU 1987-76269	19870728
AU 615416	B2	19911003		
DK 8704290	A	19880220	DK 1987-4290	19870818
AU 8941023	A	19900308	AU 1989-41023	19880901
US 5110588	A	19920505	US 1989-401403	19890901
PRIORITY APPLN. INFO.:			AU 1986-7545	A 19860819
			US 1987-86354	B2 19870817
			AU 1988-186	A 19880901
			AU 1988-1273	A 19881102

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Recombinant avirulent *Salmonella* strains contain an *Escherichia coli* DNA sequence encoding the synthesis of a lipopolysaccharide core region. These strains, unlike the parent *Salmonella* strains, can efficiently express *Vibrio cholerae* O-somatic antigen gene carried on plasmids pPM1001-4. *E. coli* EX170 (an Hfr strain with a chloramphenicol marker adjacent to the *rfa* locus, i.e. the region encoding the enzymes responsible for core lipopolysaccharide synthesis) was mated with *S. typhimurium* LB5010. Chloramphenicol *Salmonella* exconjugants which carried the *E. coli* core lipopolysaccharide on their surfaces were identified. This strain (EX200)

could express the *Vibrio cholera* O-antigen when transformed with O-antigen-encoding plasmid pEVX8 or pEVX9 (as determined by anti-*Vibrio* antiserum agglutination tests). IPCI C12N0015-00 [ICM,4]; A61K0039-108 [ICS,4]; A61K0039-112 [ICS,4];

A61K0039-106 [ICS,4]

IPCR C12N0001-20 [I,C\*]; C12N0001-20 [I,A]; A61K0039-00 [N,C\*]; A61K0039-00 [N,A]; C07K0014-195 [I,C\*]; C07K0014-28 [I,A]; C12N0015-74 [I,C\*]; C12N0015-74 [I,A]; C12R0001-01 [N,A]; C12R0001-19 [N,A]

CC 63-3 (Pharmaceuticals)

Section cross-reference(s): 15

IT *Salmonella*

*Salmonella typhi*

*Salmonella typhimurium*

(avirulent, recombinant, expression of *Vibrio cholerae*

O-antigen-synthesizing enzyme genes in)

IT Lipopolysaccharides

RL: BIOL (Biological study)

(core region of, synthesis of, genes of *Escherichia coli* for, expression in avirulent *Salmonella* of *Vibrio cholerae* O-antigen-synthesizing enzyme genes and)

IT Antigens

RL: BIOL (Biological study)

(O, of *Vibrio cholerae*, genes for synthesis of, expression in avirulent recombinant *Salmonella* of)

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD  
(2 CITINGS)

L133 ANSWER 15 OF 27 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1975:560501 CAPLUS Full-text

DOCUMENT NUMBER: 83:160501

ORIGINAL REFERENCE NO.: 83:25179a,25182a

TITLE: Membrane-associated nucleotide sugar reactions.  
Influence of mutations affecting lipopolysaccharide on the first enzyme of O-antigen synthesis

AUTHOR(S): Rundell, Kathleen; Shuster, Charles W.

CORPORATE SOURCE: Sch. Med., Case West. Reserve Univ., Cleveland, OH, USA

SOURCE: Journal of Bacteriology (1975), 123(3), 928-36

CODEN: JOBAAY; ISSN: 0021-9193

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Both the synthesis of lipopolysaccharide O-antigen and the synthesis of peptidoglycan in *Salmonella typhimurium* proceed via membrane-bound glycosylated lipid intermediates. The 1st enzyme of each pathway transfers a sugar phosphate from a nucleotide sugar to the glycosyl carrier lipid (P-GCL). Each enzyme catalyzes an exchange reaction between the reaction product UMP and the nucleotide sugar substrate. Several strains of *S. typhimurium* defective in lipopolysaccharide synthesis accumulate glycosylated lipid intermediates. In addition, strains lysogenic for phage P22 synthesize a glucose derivative of the carrier lipid. These strains were used to demonstrate the P-GCL requirement of the exchange reaction catalyzed by galactose-diphosphoglycosyl carrier lipid (GCL-PP-Gal) synthetase, the 1st enzyme of O-antigen synthesis. Enzyme activity is greatly reduced when glycosylated P-GCL accumulates on the cytoplasmic membrane. The exchange reaction catalyzed by the 1st enzyme of peptidoglycan synthesis is unaffected by the accumulation of O-antigen fragments on the carrier lipid and may interact with a different pool of P-GCL within the membrane. GCL-PP-Gal synthetase activity cannot be detected in the membranes of 2 *rfa* mutants that synthesize incomplete lipopolysaccharide core. Either the synthesis of GCL-PP-Gal synthetase or the stable integration of the enzyme into the membrane

structure may be disrupted in the rfa mutants. Peptidoglycan synthesis is unaffected by the mutations affecting the core glycosyltransferases.

CC 10-2 (Microbial Biochemistry)

Section cross-reference(s): 15

IT Antigens

RL: BIOL (Biological study)

(O, synthesis by Salmonella, membrane nucleotide effect on)

IT Salmonella typhimurium

(O-antigen synthesis by, membrane nucleotide effects on)

IT Lipopolysaccharides

RL: BIOL (Biological study)

(of Salmonella, enzymic antigen synthesis in relation to)

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD  
(4 CITINGS)

L133 ANSWER 16 OF 27 WPIX COPYRIGHT 2010 THOMSON REUTERS on STN

ACCESSION NUMBER: 2002-049352 [200206] WPIX

DOC. NO. CPI: C2002-013898 [200206]

TITLE: Microorganism useful as a vaccine for immunizing vertebrates, comprises a regulated antigen delivery system with a runaway vector and genes encoding a repressor whose synthesis is under control of an activatable control sequence

DERWENT CLASS: B04; C06; D16

INVENTOR: CURTIS R; CURTISS R; TINGE S; TINGE S A; CURTISS; TINGE A

PATENT ASSIGNEE: (AVAN-N) AVANT IMMUNOTHERAPEUTICS INC; (CURT-I) CURTIS R; (CURT-I) CURTISS R; (MEGA-N) MEGAN HEALTH INC; (TING-I) TINGE S A; (UNIW-C) UNIV WASHINGTON

COUNTRY COUNT: 93

#### PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2001083785	A2	20011108	(200206)*	EN	95	[23]
AU 2001066560	A	20011112	(200222)	EN		
EP 1292687	A2	20030319	(200322)	EN		
CN 1433474	A	20030730	(200365)	ZH		
HU 2003000793	A2	20030728	(200379)	HU		
NZ 522433	A	20040430	(200431)	EN		
ZA 2002009267	A	20040428	(200432)	EN	110	
JP 2004515210	T	20040527	(200435)	JA	168	
BR 2001010408	A	20040622	(200442)	PT		
US 20040137003	A1	20040715	(200447)	EN		
US 6780405	B1	20040824	(200457)	EN		
US 20050106176	A1	20050519	(200534)	EN		
MX 2002010690	A1	20040801	(200548)	ES		
EP 1292687	B1	20060816	(200655)	EN		
DE 60122326	E	20060928	(200664)	DE		
ES 2271031	T3	20070416	(200728)	ES		
DE 60122326	T2	20070830	(200758)	DE		
US 7341860	B2	20080311	(200820)	EN		
IN 2002DN01086	A	20100305	(201028)	EN		

#### APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
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WO 2001083785 A2	WO 2001-US13915 20010430
US 6780405 B1	US 2000-560539 20000428
US 20050106176 A1 Div Ex	US 2000-560539 20000428
US 7341860 B2 Div Ex	US 2000-560539 20000428
AU 2001066560 A	AU 2001-66560 20010430
BR 2001010408 A	BR 2001-10408 20010430
CN 1433474 A	CN 2001-810533 20010430
DE 60122326 E	DE 2001-60122326 20010430
DE 60122326 T2	DE 2001-60122326 20010430
EP 1292687 A2	EP 2001-944119 20010430
EP 1292687 B1	EP 2001-944119 20010430
DE 60122326 E	EP 2001-944119 20010430
ES 2271031 T3	EP 2001-944119 20010430
DE 60122326 T2	EP 2001-944119 20010430
JP 2004515210 T	JP 2001-580392 20010430
NZ 522433 A	NZ 2001-522433 20010430
EP 1292687 A2	WO 2001-US13915 20010430
HU 2003000793 A2	WO 2001-US13915 20010430
NZ 522433 A	WO 2001-US13915 20010430
JP 2004515210 T	WO 2001-US13915 20010430
BR 2001010408 A	WO 2001-US13915 20010430
US 20040137003 A1	WO 2001-US13915 20010430
MX 2002010690 A1	WO 2001-US13915 20010430
EP 1292687 B1	WO 2001-US13915 20010430
DE 60122326 E	WO 2001-US13915 20010430
DE 60122326 T2	WO 2001-US13915 20010430
MX 2002010690 A1	MX 2002-10690 20021028
ZA 2002009267 A	ZA 2002-9267 20021114
HU 2003000793 A2	HU 2003-793 20010430
US 20040137003 A1	US 2004-258931 20040112
US 20050106176 A1	US 2004-924574 20040824
US 7341860 B2	US 2004-924574 20040824
IN 2002DN01086 A PCT Application	WO 2001-US13915 20010430
IN 2002DN01086 A	IN 2002-DN1086 20021101

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
DE 60122326 E	Based on	EP 1292687 A
ES 2271031 T3	Based on	EP 1292687 A
DE 60122326 T2	Based on	EP 1292687 A
US 20050106176 A1	Div ex	US 6780405 B
AU 2001066560 A	Based on	WO 2001083785 A
EP 1292687 A2	Based on	WO 2001083785 A
HU 2003000793 A2	Based on	WO 2001083785 A
NZ 522433 A	Based on	WO 2001083785 A
JP 2004515210 T	Based on	WO 2001083785 A
BR 2001010408 A	Based on	WO 2001083785 A
MX 2002010690 A1	Based on	WO 2001083785 A
EP 1292687 B1	Based on	WO 2001083785 A
DE 60122326 E	Based on	WO 2001083785 A
DE 60122326 T2	Based on	WO 2001083785 A
US 7341860 B2	Div ex	US 6780405 B

PRIORITY APPLN. INFO:	US 2000-560539	20000428
	US 2004-258931	20040112
	US 2004-924574	20040824

INT. PATENT CLASSIF.:

MAIN: C12N015-09; C12N015-63  
 SECONDARY: A61K039-00; A61K039-112; A61P037-04; C12N001-21;  
 C12P021-02  
 IPC ORIGINAL: A61K0039-00 [I,A]; A61K0039-00 [I,A]; A61K0039-00 [I,C];  
 A61K0045-00 [I,A]; A61K0045-00 [I,A]; A61K0045-00 [I,C];  
 C12N0001-20 [I,A]; C12N0001-20 [I,C]; C12N0001-21 [I,A];  
 C12N0001-21 [I,A]; C12N0001-21 [I,C]; C12N0015-63 [I,C];  
 C12N0015-63 [I,A]; C12N0015-63 [I,A]; C12N0015-63 [I,C];  
 C12N0015-74 [I,A]; C12N0015-74 [I,A]; C12N0015-74 [I,C];  
 C12P0021-06 [I,A]; C12P0021-06 [I,C]  
 IPC RECLASSIF.: A01N0063-00 [I,A]; A01N0063-00 [I,C]; A61K0039-00 [I,A];  
 A61K0039-00 [I,C]; A61K0039-00 [I,A]; A61K0039-00 [I,C];  
 A61K0039-112 [I,A]; A61K0039-112 [I,C]; A61K0039-38 [I,A]  
 ; A61K0039-38 [I,C]; A61K0048-00 [I,A]; A61K0048-00 [I,C]  
 ; A61P0037-00 [I,C]; A61P0037-04 [I,A]; C12N0001-21 [I,A]  
 ; C12N0001-21 [I,C]; C12N0015-09 [I,A]; C12N0015-09 [I,C]  
 ; C12N0015-63 [I,A]; C12N0015-63 [I,C]; C12N0015-74 [I,A]  
 ; C12N0015-74 [I,C]; C12P0021-02 [I,A]; C12P0021-02 [I,C]  
 ; C12R0001-42 [N,A]  
 ECLA: A61K0039-02M; A61K0039-09A; C12N0015-63A; C12N0015-74  
 ICO: K61K0039:52B; K61K0039:52C; K61K0039:53; K61K0039:54A2;  
 K61K0039:55V; K61K0039:55B7  
 USCLASS NCLM: 424/093.100; 424/184.100; 424/200.100  
 NCLS: 424/093.200; 424/093.400; 424/200.100; 435/252.300;  
 435/320.100; 435/471.000  
 JAP. PATENT CLASSIF.:  
 MAIN/SEC.: A61K0039-00 H; A61K0039-112; A61P0037-04; C12N0001-21;  
 C12N0015-00 A (ZNA); C12P0021-02 C  
 FTERM CLASSIF.: 4B024; 4B064; 4B065; 4C085; 4C201; 4B024/AA01;  
 4C085/AA03; 4B024/AA11; 4B065/AA46.X; 4B065/AB01;  
 4B064/AG31; 4B065/BA02; 4C085/BA24; 4B024/BA80;  
 4B064/CA02; 4B024/CA04; 4B064/CA19; 4B065/CA24;  
 4B065/CA45; 4C085/CC07; 4B064/CC24; 4B064/DA01;  
 4B024/DA06; 4C085/DD01; 4B024/EA04; 4C085/EE01;  
 4B024/GA11; 4B024/HA12

## BASIC ABSTRACT:

WO 2001083785 A2 UPAB: 20100430

NOVELTY - A microorganism (I) comprising a regulated antigen delivery system (RADS), comprising: (a) a vector (II) having: (i) a site (SI) for insertion of a desired gene; and (ii) a first origin of replication (ori) and a second ori conferring vector replication using DNA polymerase III and I, respectively; and

(b) a gene (III) encoding a first repressor (FR) operably linked to a first activatable control sequence, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a runaway vector (IV) comprising (II); (2) producing a desired gene product comprising: (a) engineering a gene encoding the desired product into the vector of (I), where the microorganism comprises control sequences that repress expression of the second ori under an environmental condition, but in which the expression of the second ori is derepressed under a second environmental condition;

(b) culturing (I) under the first environmental condition; and (c) culturing the microorganism with the vector of (a) under the second environmental condition;

(3) a vaccine (V) for immunization of a vertebrate, where (V) comprises (I) in a carrier;

(4) inducing immunoprotection in a vertebrate comprising administering (V); and

(5) delivering a desired gene product to a vertebrate comprising administering (I).

ACTIVITY - Antibacterial; immunostimulant.

MECHANISM OF ACTION - Vaccine (claimed). The immunogenic properties of the RAV SeM vaccine strains were initially evaluated in BALB/c mice given about 10<sup>7</sup> colony forming units (CFU) of each strain intranasally on day 0 and day 28 without anesthesia. Only low levels of vaccine strains were recovered from the Lungs and Peyer's patches of the immunized mice 72 hours following immunization and similarly were rarely detected in feces of immunized mice following day 3. The serological immunoglobulin (Ig)G SeM specific antibody response detected indicated that all strains induced strong antibody immune response to the SeM antigen.

USE - (I) is useful for producing a desired gene product, preferably an antigen which is Ery65 or SeM. (I) is useful for delivering a desired gene product in a vertebrate. A vaccine (V) comprising (I) is useful for inducing immunoprotection in a vertebrate against antigens such as Ery65 which causes disease erysipelas and in later life can cause arthritis in swine and turkeys, and SeM which causes strangles in racehorses and other equines (all claimed).

ADVANTAGE - As a vaccine, the RADS is capable of causing an effective exposure of the immunized vertebrate's lymphoid tissues to a large dose of vector-encoded foreign gene product production in response to the withdrawal of the stimulus. The RADS microorganism can be grown in vitro under low copy number control, then switched to runaway conditions after vertebrate inoculation to cause an increase in antigen production in vivo. Under derepressed runaway conditions, the RADS microorganisms is highly impaired due to extremely high plasmid replication activity coupled with extremely high foreign gene product production. Because of its impaired state, the derepressed RADS microorganisms cannot generally survive for extended periods.

#### TECHNOLOGY FOCUS:

BIOTECHNOLOGY - Preferred Microorganism: (I) further comprises a gene encoding a desired gene product inserted into SI, where the gene encoding the desired gene product is operably linked to a second control sequence and where the first control sequence and the second control sequences are the same sequence or different sequences. The repressor is from LacI repressor and C2 repressor and the second control sequence is repressible by a second repressor. Preferably (I), which is an attenuated derivative of pathogenic bacterium, preferably *Salmonella* sp. comprises a plasmid pMEG-771 as (II). The gene product is an antigen preferably *Erysipelothrix rhusiopathiae* (Ery65) or *Streptococcus equi* (SeM), where the first activatable control sequence is *araCPBAD*, pSC ori and pUC ori as first and second ori respectively, P22 PR as first control sequence and C2 repressor as first repressor, P<sub>trc</sub> as a second control sequence where the sequence is repressible by a second repressor which is a LacI repressor. The desired gene product is operably linked to an eukaryotic control sequence. The microorganism further comprises a balanced lethal host vector system consisting of a lack of a functioning essential gene on the chromosome and a recombinant functioning copy of the essential gene on (II), where the essential gene is an *asd* gene which is preferably inactivated by the insertion of a repressor gene operably linked to *araCPBAD*. The microorganisms further comprise an inactivating mutation in a native gene selected from *cya*, *crp*, *phoPQ*, *ompR*, *galE*, *cdt*, *hemA*, *aroA*, *aroC*, *aroD* and *htrA*. The modified form of the microorganism further comprises an *DELTAendA* mutation. The microorganism exhibits delayed RADS characteristics, where the delayed RADS characteristics are conferred by an alteration selected from mutations that delay the loss of activator molecules by metabolism and/or leakage, a mutation or insertion to increase repressor concentration, and inclusion of a vector control sequence with binding sites for more than repressor and/or vector sequences encoding repressor molecules that act on a vector control sequence.

Preferred Method: In (2), the first environmental condition comprises the presence of arabinose and in vitro culture conditions, and

the second environmental condition comprises the absence of arabinose and conditions inside a vertebrate and a microorganism further comprising the inactivation deletion in the araCBAD operon and/or the araE gene

Production: (I) is produced by standard recombinant techniques.

#### EXTENSION ABSTRACT:

ADMINISTRATION - Administration of a vaccine (V) comprising (I) is oral, intranasal, gastric intubation or in the form of aerosols, although other methods of administering the antigen delivery microorganism are by intravenous, intramuscular, subcutaneous, intramammary, intrapenial, intrarectal or vaginal routes. Dosage of (V) is  $1 \times 10$  to the power of 7 -  $1 \times 10$  to the power of 11 colony forming units (CFU). EXAMPLE - The runaway vector (RAV) pMEG-573 encoding the *Streptococcus equi* SeM protein was obtained by cloning the polymerase chain reaction (PCR) fragment flanked by primers SeM444-474 GCGAACTCTGAGGTTAGTCGTACGGCGACTC and sEM1265-1233 TTGATCAATTCTGCTAATTTTGTAGCCATTTC, containing the central portion of the SeM coding region from the SeM clone pSEM06, into the NcoI and BamHI sites of pMEG-546. pMEG-573 was only dependent on the presence of the DELTAilvG3::TTaraCPBADlacIT deletion/insertion mutation in the chromosome to repress the runaway phenotype and SeM expression. The vaccine strains for SeM also contained either the DELTAphoP1918 or DELTAphoP24 attenuating deletion mutation. A comparison of the level of SeM expression by different attenuated *Salmonella* vaccine strains, in which SeM expression on the plasmid vector was under the transcriptional control of either P22 PR, Ptrc or lambdaPL on pBR based plasmids, or under the control of Ptrc on the RAV, pMEG-573. Strains for this comparison were grown in Luria bertani broth for 6 hours either with or without 0.2 % arabinose following a 1/1000 dilution from non-aerated Luria Bertani broth cultures with 0.2 % arabinose. 1 ml of cells were then pelleted and total proteins were run on sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) for analysis by staining with Coomassie blue or transfer to nitrocellulose for western blot analysis with SeM specific antibody. The analysis showed that the amount of the SeM protein was substantially more in the bacterial strain, MGN-4598 (pMEG-573), with the RAV pMEG-573 than present in any of the other host-vector strains. Given that all plasmids in these strains contain the same SeM coding region found in pMEG-375, and the level of SeM expression obtained is not detectable on the Coomassie gel with any of the other strong promoters tested in MGN-4598 (pMEG-825) P22 PR, MGN-4598 (pMEG-826) Ptrc or -2238 (pMEG-575) lambda PL (all on pBR based plasmids), only the RAV constructs were ever evaluated in animals.

FILE SEGMENT: CPI

MANUAL CODE: CPI: B04-B04C1; B04-E03; B04-E03B; B04-E04; B04-E08;  
B04-F0100E; B04-F10A8E; B04-N0300E; B04-P0100E; B14-A01;  
B14-G01; C04-B04C1; C04-E03; C04-E03B; C04-E04; C04-E08;  
C04-F0100E; C04-F10A8E; C04-N0300E; C14-A01; C14-G01;  
D05-H07; D05-H12E; D05-H14A; D05-H16A; D05-H17

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STN DUPLICATE 1

ACCESSION NUMBER: 2009:183097 BIOSIS Full-text

DOCUMENT NUMBER: PREV200900183097

TITLE: *Salmonella enterica* Serovar Typhimurium Strains  
with Regulated Delayed Attenuation In Vivo.

AUTHOR(S): Curtiss, Roy III [Reprint Author]; Wanda, Soo-Young; Gunn,  
Bronwyn M.; Zhang, Xin; Tinge, Steven A.; Ananthnarayan,  
Vidya; Mo, Hua; Wang, Shifeng; Kong, Wei

CORPORATE SOURCE: Arizona State Univ, Biodesign Inst, Ctr Infect Dis and  
Vaccinol, POB 857401, Tempe, AZ 85287 USA  
rcurtiss@asu.edu

SOURCE: Infection and Immunity, (MAR 2009) Vol. 77, No. 3, pp. 1071-1082.

CODEN: INFIBR. ISSN: 0019-9567.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 11 Mar 2009

Last Updated on STN: 11 Mar 2009

ABSTRACT: Recombinant bacterial vaccines must be fully attenuated for animal or human hosts to avoid inducing disease symptoms while exhibiting a high degree of immunogenicity. Unfortunately, many well-studied means for attenuating \*\*\*Salmonella\*\*\* render strains more susceptible to host defense stresses encountered following oral vaccination than wild-type virulent strains and/or impair their ability to effectively colonize the gut-associated and internal lymphoid tissues. This thus impairs the ability of recombinant vaccines to serve as factories to produce recombinant antigens to induce the desired protective immunity. To address these problems, we designed strains that display features of wild-type virulent strains of *Salmonella* at the time of immunization to enable strains first to effectively colonize lymphoid tissues and then to exhibit a regulated delayed attenuation in vivo to preclude inducing disease symptoms. We recently described one means to achieve this based on a reversible smooth-rough synthesis of lipopolysaccharide O

\*\*\*antigen.\*\*\* We report here a second means to achieve regulated delayed attenuation in vivo that is based on the substitution of a tightly regulated *araC* P BAD cassette for the promoters of the *fur*, *crp*, *phoPQ*, and *rpoS* genes such that expression of these genes is dependent on arabinose provided during growth. Thus, following colonization of lymphoid tissues, the *Fur*, *Crp*, *PhoPQ*, and/or *RpoS* proteins cease to be synthesized due to the absence of arabinose such that attenuation is gradually manifest in vivo to preclude induction of disease symptoms. Means for achieving regulated delayed attenuation can be combined with other mutations, which together may yield safe efficacious recombinant attenuated *Salmonella* vaccines.

CONCEPT CODE: Genetics - General 03502  
Genetics - Animal 03506  
Biochemistry studies - Carbohydrates 10068  
Pathology - Therapy 12512  
Digestive system - Physiology and biochemistry 14004  
Blood - Blood and lymph studies 15002  
Blood - Blood cell studies 15004  
Pharmacology - General 22002  
Pharmacology - Immunological processes and allergy 22018  
Physiology and biochemistry of bacteria 31000  
Genetics of bacteria and viruses 31500  
Immunology - General and methods 34502  
Medical and clinical microbiology - Bacteriology 36002

INDEX TERMS: Major Concepts  
Pharmacology; Infection; Immune System (Chemical Coordination and Homeostasis); Molecular Genetics (Biochemistry and Molecular Biophysics)

INDEX TERMS: Parts, Structures, & Systems of Organisms  
gut: digestive system; lymphoid tissue: blood and lymphatics

INDEX TERMS: Diseases  
*Salmonella enterica* infection: bacterial disease, prevention and control

INDEX TERMS: Chemicals & Biochemicals  
recombinant antigen; arabinose; *Fur* protein; *RpoS* protein; lipopolysaccharide O antigen  
; recombinant bacterial vaccine: immunologic-drug, immunostimulant-drug, pharmacodynamics, vaccine; *Crp* protein; *PhoPQ* protein

INDEX TERMS: Methods & Equipment  
immunization: therapeutic and prophylactic techniques,  
clinical techniques; oral vaccination: therapeutic and  
prophylactic techniques, clinical techniques

INDEX TERMS: Miscellaneous Descriptors  
protective immunity; colonization; immunogenicity;  
delayed attenuation; host defense stress

ORGANISM: Classifier  
Enterobacteriaceae 06702  
Super Taxa  
Facultatively Anaerobic Gram-Negative Rods; Eubacteria;  
Bacteria; Microorganisms  
Organism Name  
Salmonella enterica (species): pathogen, 23  
strains, serovar-Typhimurium  
Taxa Notes  
Bacteria, Eubacteria, Microorganisms

ORGANISM: Classifier  
Muridae 86375  
Super Taxa  
Rodentia; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
mouse (common): immature, host, strain-BALB/c,  
strain-C57BL/6, female  
Taxa Notes  
Animals, Chordates, Mammals, Nonhuman Vertebrates,  
Nonhuman Mammals, Rodents, Vertebrates

REGISTRY NUMBER: 147-81-9 (arabinose)

GENE NAME: Salmonella enterica fur gene  
(Enterobacteriaceae): expression; Salmonella  
enterica rpoS gene (Enterobacteriaceae): expression;  
Salmonella enterica crp gene (Enterobacteriaceae):  
expression; Salmonella enterica phoPQ gene  
(Enterobacteriaceae): expression

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STN DUPLICATE 5

ACCESSION NUMBER: 2007:242492 BIOSIS Full-text

DOCUMENT NUMBER: PREV200700237077

TITLE: Role of RpoS in fine-tuning the synthesis of Vi capsular  
polysaccharide in Salmonella enterica serotype  
Typhi.

AUTHOR(S): Santander, Javier; Wanda, Soo-Young; Nickerson, Cheryl A.;  
Curtiss, Roy III [Reprint Author]

CORPORATE SOURCE: Arizona State Univ, Biodesign Inst, Ctr Infect Dis and  
Vaccinol, POB 875401, 1001 S McAllister Ave, Tempe, AZ 85287  
USA  
rcurtiss@asu.edu

SOURCE: Infection and Immunity, (MAR 2007) Vol. 75, No. 3, pp.  
1382-1392.  
CODEN: INFIBR. ISSN: 0019-9567.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 11 Apr 2007  
Last Updated on STN: 11 Apr 2007

ABSTRACT: Regulation of the synthesis of Vi polysaccharide, a major virulence  
determinant in Salmonella enterica serotype Typhi, is under the  
control of two regulatory systems, ompR-envZ and rscB-rscC, which respond to  
changes in osmolarity. Some serotype Typhi strains exhibit overexpression of  
Vi polysaccharide, which masks clinical detection of lipopolysaccharide 0

antigen. This variation in Vi polysaccharide and O antigen display (VW variation) has been observed since the initial studies of serotype Typhi. In this study, we report that *rpoS* plays a role in this increased expression in Vi polysaccharide. We constructed a variety of isogenic serotype Typhi mutants that differed in their expression levels of *RpoS* and examined the role of the *rpoS* product in synthesis of Vi polysaccharide under different osmolarity conditions. Vi polysaccharide synthesis was also examined in serotype Typhi mutants in which the native promoter of the *rpoS* was replaced by an \*\*\*araCP\*\*\* (EAD) cassette, so that the expression of *rpoS* was arabinose dependent. The *RpoS*(-) strains showed increased syntheses of Vi polysaccharide, which at low and medium osmolarities masked O antigen detection. In contrast, *RpoS*(+) strains showed lower syntheses of Vi polysaccharide, and an increased detection of O antigen was observed. During exponential growth, when *rpoS* is unstable or present at low levels, serotype Typhi *RpoS*(+) strains overexpress the Vi polysaccharide at levels comparable to those for *RpoS*- strains. Our results show that *RpoS* is another regulator of Vi polysaccharide synthesis and contributes to VW variation in serotype Typhi, which has implications for the development of recombinant attenuated \*\*\*Salmonella\*\*\* vaccines in humans.

CONCEPT CODE: Genetics - General 03502  
 Biochemistry studies - Carbohydrates 10068  
 Physiology and biochemistry of bacteria 31000  
 Genetics of bacteria and viruses 31500

INDEX TERMS: Major Concepts  
 Molecular Genetics (Biochemistry and Molecular Biophysics)

INDEX TERMS: Chemicals & Biochemicals  
 arabinose; *RpoS*; O antigen; Vi capsular polysaccharide: synthesis

ORGANISM: Classifier  
 Enterobacteriaceae 06702  
 Super Taxa  
 Facultatively Anaerobic Gram-Negative Rods; Eubacteria; Bacteria; Microorganisms  
 Organism Name  
*Salmonella enterica* (species): serotype typhi  
 Taxa Notes  
 Bacteria, Eubacteria, Microorganisms

REGISTRY NUMBER: 147-81-9 (arabinose)

GENE NAME: *Salmonella enterica rpoS* gene  
 (Enterobacteriaceae): mutation, expression;  
*Salmonella enterica araCP-EAD*  
 gene (Enterobacteriaceae): mutation, expression

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ACCESSION NUMBER: 2002:176652 BIOSIS Full-text  
 DOCUMENT NUMBER: PREV200200176652  
 TITLE: Cloning and characterization of an iron regulated locus, *iroA*, in *Salmonella choleraesuis*.  
 AUTHOR(S): Chang, C. F. [Reprint author]; Wu, W. S. [Reprint author]; Hsieh, P. C. [Reprint author]; Chang, Y. F. [Reprint author]  
 CORPORATE SOURCE: National Taiwan University, Taipei, Taiwan  
 SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 125. print.  
 Meeting Info.: 101st General Meeting of the American Society for Microbiology. Orlando, FL, USA. May 20-24, 2001. American Society for Microbiology.  
 ISSN: 1060-2011.

DOCUMENT TYPE: Conference; (Meeting)  
 Conference; Abstract; (Meeting Abstract)  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: 6 Mar 2002  
 Last Updated on STN: 6 Mar 2002

ABSTRACT: The ability of *Salmonella choleraesuis* to acquire iron in an iron-restricted environment from the host has been shown to correlate with virulence. This bacterium has evolved a high-affinity iron acquisition system and many iron transport genes are regulated by iron. In many bacteria, transcriptional regulation by iron depends on the ferric \*\*\*uptake\*\*\* regulator, the *fur* gene. In order to identify the Fur regulated-iron acquisition genes of *S. choleraesuis*, we have used the Fur titration assay (FURTA) to screen the Fur regulated promoters regions and then, to compare with *Escherichia coli* Fur box consensus sequence. The DNA sequence of a positive FURTA clone (pSC4) shows homologous to *iroB* gene in the *iroA* locus of *S. typhimurium*. DNA probe derived from this clone has been used to screen a lambda-dash library of *S. choleraesuis*. The *iroA* locus of *S. choleraesuis* has been cloned and sequenced. The DNA sequence results revealed that the *iroA* locus consists of *iroB*, C, D, E, and N genes. The DNA sequence of the *iron* gene showed homologous to several TonB-dependent \*\*\*outer\*\*\* membrane siderophore receptors and putative virulence gene among the extraintestinal pathogenic *E. coli*. Further characterization of the in vivo expression of *Iron* polypeptides and the pathogenicity of its knockout mutant in an animal model is in progress.

CONCEPT CODE: General biology - Symposia, transactions and proceedings  
 00520

Genetics - General 03502

Biochemistry studies - Minerals 10069

Physiology and biochemistry of bacteria 31000

Genetics of bacteria and viruses 31500

INDEX TERMS: Major Concepts  
 Molecular Genetics (Biochemistry and Molecular Biophysics)

INDEX TERMS: Chemicals & Biochemicals  
 Iron polypeptides: expression; iron

INDEX TERMS: Methods & Equipment  
 Fur titration assay: detection method; cloning:  
 molecular genetic method

INDEX TERMS: Miscellaneous Descriptors  
 iron-restricted environment; transcriptional regulation;  
 virulence; Meeting Abstract

REGISTRY NUMBER: 7439-89-6 (iron)

GENE NAME: *Salmonella chloeraesuis iroA* gene  
 (Enterobacteriaceae); *Salmonella choleraesuis*  
*fur* gene [*Salmonella*  
*choleraesuis* ferric uptake  
 regulator gene] (Enterobacteriaceae)

L133 ANSWER 20 OF 27 BIOTECHDS COPYRIGHT 2010 THOMSON REUTERS on STN

ACCESSION NUMBER: 1991-09175 BIOTECHDS Full-text

TITLE: Vaccine protecting against Gram-negative bacterium;  
 comprises attenuated *Salmonella*  
*typhimurium* with deletion in e.g. adenylate-cyclase,  
 cyclic AMP receptor gene

PATENT ASSIGNEE: Washington-Univ.

PATENT INFO: WO 9106317 16 May 1991

APPLICATION INFO: WO 1990-US6503 2 Nov 1990

PRIORITY INFO: US 1989-431597 3 Nov 1989

DOCUMENT TYPE: Patent

LANGUAGE: English



OTHER SOURCE: WPI: 1991-163958 [22]  
 ABSTRACT: A vaccine for protection against Gram-negative bacteria contains a live, avirulent *Salmonella* able to induce immunity to homologous and heterologous *Salmonella* serotypes and other Gram-negative enteric bacteria. The *Salmonella* has at least 1 mutation in a gene which globally regulates other genes, and a second mutation in a gene encoding an enzyme involved in lipopolysaccharide synthesis, which results in a reversible rough phenotype. The second mutation may be in a gene (phoP) which regulates synthesis of iron-regulated outer membrane proteins (OMP) and results in constitutive expression of OMP. The isolated avirulent strains of *Salmonella typhimurium* carrying the specified mutations are claimed, and are selected from Chi3761, Chi3985, Chi4126, Chi4137 and Chi4152. The preferred organisms have mutations, especially deletions, in the adenylate-cyclase (EC-4.6.1.1) gene (cya) and in the cyclic-AMP receptor protein gene (crp) (involved in global regulation). The second mutation is in the gale (UDP-galactose-epimerase) or pmi (mannosephosphate-isomerase, EC-5.3.1.8) genes to impart the reversibly rough phenotype, or is in the fur gene. (67pp)

CLASSIFICATION: D PHARMACEUTICALS; D4 Vaccines; A MICROBIOLOGY; A1 Genetics  
 CONTROLLED TERMS: AVIRULENT SALMONELLA TYPHIMURIUM APPL. VACCINE  
 PREP., ATTENUATION BY DELETION IN  
 ADENYLATE-CYCLASE, CYCLIC-AMP RECEPTOR,  
 UDP-GALACTOSE-EPIMERASE, MANNOSEPHOSPHATE-ISOMERASE GENE  
 BACTERIUM ENZYME EC-4.6.1.1 EC-5.3.1.8

L133 ANSWER 21 OF 27 SCISEARCH COPYRIGHT (c) 2010 The Thomson Corporation on  
 STN DUPLICATE 8

ACCESSION NUMBER: 1992:403572 SCISEARCH Full-text  
 THE GENUINE ARTICLE: JB456  
 TITLE: EFFECT OF SALMONELLA-TYPHIMURIUM FERRIC  
 UPTAKE REGULATOR (FUR) MUTATIONS  
 ON IRON-REGULATED AND PH-REGULATED PROTEIN-SYNTHESIS  
 AUTHOR: FOSTER J W (Reprint)  
 CORPORATE SOURCE: UNIV SO ALABAMA, COLL MED, DEPT MICROBIOL & IMMUNOL,  
 MOBILE, AL 36688 (Reprint)  
 AUTHOR: HALL H K  
 COUNTRY OF AUTHOR: USA  
 SOURCE: JOURNAL OF BACTERIOLOGY, (JUL 1992) Vol. 174, No. 13, pp.  
 4317-4323.  
 ISSN: 0021-9193.  
 PUBLISHER: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW,  
 WASHINGTON, DC 20005-4171.  
 DOCUMENT TYPE: Article; Journal  
 FILE SEGMENT: LIFE  
 LANGUAGE: English  
 REFERENCE COUNT: 41  
 ENTRY DATE: Entered STN: 1994  
 Last Updated on STN: 1994

ABSTRACT:

Fur is an important regulatory protein known to function in the presence of iron as a repressor of iron-controlled genes. It was recently discovered that Fur is also essential to *Salmonella typhimurium* for mounting an adaptive acid tolerance response (J. W. Foster, J. Bacteriol 173:6896-6902, 1991). Because little is known about the effect of Fur on the physiology of this enteric pathogen, a systematic two-dimensional polyacrylamide gel electrophoresis (PAGE) analysis was conducted to identify proteins whose synthesis is linked to iron levels. Mutations in the

fur locus were identified and used to classify which proteins are controlled by Fur. Thirty-six proteins were overtly affected by iron availability, most of which were clearly under the control of Fur. Although most of the Fur-dependent proteins were under negative control, a significant portion (15 of 34) appeared to be under a form of positive control. Nine of the positively controlled proteins required Fur and iron for expression. However, Fur lacking iron was also required for the induction of six gene products. Surprisingly, not all iron-regulated proteins were controlled by Fur and not all Fur-dependent proteins were obviously regulated by iron status. Because fur mutants fail to mount an effective acid tolerance response, we made a comparative two-dimensional PAGE analysis of 100 total acid- and iron-regulated gene products. Production of most of these proteins was regulated by only one of the two stresses, yet a clear subset of seven genes were influenced by both acid and iron and were also controlled by fur. These proteins were also members of the acid tolerance response modulon. Consistent with the fur effect on pH-regulated protein synthesis, fur mutants lacked the inducible pH homeostasis system associated with the acid tolerance response. The results provide further evidence that Fur has an extensive impact on gene expression and cellular physiology and suggest an explanation for the acid-sensitive nature of fur mutants.

CATEGORY: MICROBIOLOGY

SUPPL. TERM PLUS: CAMP RECEPTOR PROTEIN; ESCHERICHIA-COLI; GENE-EXPRESSION; OUTER-MEMBRANE; TRANSPORT; REPRESSOR; OPERON; VIRULENCE; OPERATOR; SYSTEMS

REFERENCE(S) :

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG  (RPG)	Referenced Work (RWK)
AIBA, H	1983	32	141	CELL
AIBA, H	1985	4	3329	EMBO J
AIBA, H	1985	260	3063	J BIOL CHEM
ALIABADI, Z	1988	170	842	J BACTERIOL
BAGG, A	1987	26	5471	BIOCHEMISTRY-US
BAGG, A	1987	51	509	MICROBIOL REV
BENJAMIN, W H	1985	50	392	INFECT IMMUN
BENNETT, R L	1976	127	498	J BACTERIOL
BOOTH, I R	1979	182	687	BIOCHEM J
BOYD, J	1990	87	5968	P NATL ACAD SCI USA
CALDERWOOD, S B	1987	169	4759	J BACTERIOL
CHUMLEY, F G	1979	91	639	GENETICS
CROSA, J H	1989	53	517	MICROBIOL REV
DAVIS, R W	1980			ADV BACTERIAL GENETI
DELORENZO, V	1987	169	2624	J BACTERIOL
DUBOS, R J	1946	84	143	J EXP MED
ERNST, J F	1978	135	928	J BACTERIOL
FINLAY, B B	1989	53	210	MICROBIOL REV
FOSTER, J W	1990	172	771	J BACTERIOL
FOSTER, J W	1991	173	5129	J BACTERIOL
FOSTER, J W	1991	173	6896	J BACTERIOL
FOSTER, J W				UNPUB
GARGES, S	1988	170	1417	J BACTERIOL
GOLDBERG, M B	1991	88	1125	P NATL ACAD SCI USA
HANTKE, K	1987	210	135	MOL GEN GENET
HENNECKE, H	1990	4	1621	MOL MICROBIOL
HOLLEY, E A	1982	152	959	J BACTERIOL
MALLICK, U	1979	76	5520	P NATL ACAD SCI USA
MILLER, J H	1972			EXPT MOL GENETICS
NEIDERHOFFER, E C	1990	172	1930	J BACTERIOL
NEILANDS, J B	1982	36	285	ANNU REV MICROBIOL
NEILANDS, J B	1972	11	145	STRUCT BONDING BERLI

PAYNE, S M	1988	16	81	CRC CRIT R MICROBIOL
SANDERSON, K E	1988	52	485	MICROBIOL REV
SPECTOR, M				COMMUNICATION
SPECTOR, M P	1986	168	420	J BACTERIOL
SPECTOR, M P	1988	170	345	J BACTERIOL
STAGGS, T M	1991	173	417	J BACTERIOL
STOEBNER, J A	1988	56	2891	INFECT IMMUN
VOGEL, H J	1956	218	97	J BIOL CHEM
WANNER, B L	1986	191	39	J MOL BIOL

L133 ANSWER 22 OF 27 SCISEARCH COPYRIGHT (c) 2010 The Thomson Corporation on  
STN

ACCESSION NUMBER: 1998:776862 SCISEARCH Full-text

THE GENUINE ARTICLE: 127JD

TITLE: Iron-responsive gene regulation in a *Campylobacter jejuni*  
fur mutant

AUTHOR: Ketley J M (Reprint)

CORPORATE SOURCE: Univ Leicester, Dept Genet, Univ Rd, Leicester LE1 7RH,  
Leics, England (Reprint)

AUTHOR: van Vliet A H M; Wooldridge K G

CORPORATE SOURCE: Univ Leicester, Dept Genet, Leicester LE1 7RH, Leics,  
England

COUNTRY OF AUTHOR: England

SOURCE: JOURNAL OF BACTERIOLOGY, (OCT 1998) Vol. 180, No. 20, pp.  
5291-5298.

ISSN: 0021-9193.

PUBLISHER: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC  
20036-2904 USA.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 64

ENTRY DATE: Entered STN: 1998

Last Updated on STN: 1998

#### ABSTRACT:

The expression of iron-regulated systems in gram-negative bacteria is generally controlled by the Fur protein, which represses the transcription of iron-regulated promoters by using Fe<sup>2+</sup> as a cofactor. Mutational analysis of the *Campylobacter jejuni* fur gene was carried out by generation of a set of mutant copies of fur which had a kanamycin or chloramphenicol resistance gene introduced into the regions encoding the N and C termini of the Fur protein. The mutated genes were recombined into the *C. jejuni* NCTC 11168 chromosome, and putative \*\*\*mutants\*\*\* were confirmed by Southern hybridization. *C. jejuni* \*\*\*mutants\*\*\* were obtained only when the resistance genes were transcribed in the same orientation as the fur gene. The *C. jejuni* fur mutant grew slower than the parental strain. Comparison of protein profiles of fractionated *C. jejuni* cells grown in low- or high-iron medium indicated derepressed expression of three iron-regulated outer \*\*\*membrane\*\*\* proteins with molecular masses of 70, 75, and 80 kDa. Characterization by N-terminal amino acid sequencing showed the 75-kDa protein to be identical to CfrA, a *Campylobacter* coil siderophore receptor homologue, whereas the 70 kDa protein was identified as a new siderophore receptor homologue. Periplasmic fractions contained four derepressed proteins with molecular masses of 19, 29, 32, and 36 kDa. The 19-kDa protein has been previously identified, but its function is unknown. The cytoplasmic fraction contained two iron-repressed and two iron-induced proteins with molecular masses of 26, 55, 31, and 40 kDa, respectively. The two iron-repressed proteins have been previously identified as the oxidative stress defense proteins catalase (KatA) and alkyl hydroperoxide reductase (AhpC). AhpC and KatA were still iron regulated in the fur mutant, suggesting the

presence of Fur-independent iron regulation. Further analysis of the C, jejuni iron and Fur regulons by using two-dimensional gel electrophoresis demonstrated the total number of iron- and Fur-regulated proteins to be loner than for other bacterial pathogens.

CATEGORY: MICROBIOLOGY  
 SUPPL. TERM PLUS: FERRIC UPTAKE REGULATOR;  
 OUTER-MEMBRANE PROTEIN;  
 ESCHERICHIA-COLI; SALMONELLA-TYPHIMURIUM;  
 PSEUDOMONAS-AERUGINOSA; MOLECULAR CHARACTERIZATION;  
 NEISSERIA-MENINGITIDIS; SUPEROXIDE-DISMUTASE;  
 NUCLEOTIDE-SEQUENCE; FUNCTIONAL DOMAINS

## REFERENCE(S):

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
AUSUBEL F M	1992			SHORT PROTOCOLS MOL
BAILLON M L A				UNPUB CHARACTERISATI
BERISH S A	1993	61	4599	INFECT IMMUN
BLASER M J	1983	5	157	EPIDEMIOLOG REV
BOURKE B B	1996	183	219	GENE
BSAT N	1998	29	189	MOL MICROBIOL
BULLEN J J	1981	3	1127	REV INFECT DIS
CHAN V L	1995	164	25	GENE
CHAN V L	1992	174	695	J BACTERIOL
CHAN V L	1991	101	51	GENE
CHATTERJEE S	1998			UNPUB
CHRISTMAN M F	1989	86	3484	P NATL ACAD SCI USA
COY M	1991	30	8201	BIOCHEMISTRY-US
DUBBELS B				COMMUNICATION
ERNST J F	1978	135	928	J BACTERIOL
FARR S B	1991	55	561	MICROBIOL REV
FIELD L H	1986	54	126	INFECT IMMUN
FOSTER J W	1992	174	4317	J BACTERIOL
GRANT K A	1995	141	1369	MICROBIOL-UK
GUERRY P	1997	179	3997	J BACTERIOL
HANTKE K	1984	197	337	MOL GEN GENET
HANTKE K	1987	210	135	MOL GEN GENET
HASSETT D J	1996	178	3996	J BACTERIOL
JANVIER B				IN PRESS RES MICROBI
KARKHOFFSCHWEIZ.RR	1994	141	139	GENE
KARLYSHEV A V	1998	144	503	MICROBIOL-UK 2
KETLEY J M	1997	143	5	MICROBIOL-UK 1
LITWIN C M	1992	174	1897	J BACTERIOL
LITWIN C M	1994	176	240	J BACTERIOL
LITWIN C M	1993	175	706	J BACTERIOL
LITWIN C M	1993	6	137	CLIN MICROBIOL REV
MILLER J F	1988	85	856	P NATL ACAD SCI USA
MISHU B	1993	17	104	CLIN INFECT DIS
MONGKOLSUK S	1997	179	3950	J BACTERIOL
OCHSNER U A	1996	93	4409	P NATL ACAD SCI USA
PARK S F	1995	177	2259	J BACTERIOL
PARK S F				COMMUNICATION
PICKETT C L	1992	60	3872	INFECT IMMUN
PRINCE R W	1993	175	2589	J BACTERIOL
RICHARDSON P T	1995	141	3181	MICROBIOL-UK 12
RIDOUT C J	1995	365	152	FEBS LETT
SAMBROOK J	1989			MOL CLONING LAB MANU
SCHAFFER S	1985	200	110	MOL GEN GENET
STAGGS T M	1991	173	417	J BACTERIOL
STAGGS T M	1994	176	7614	J BACTERIOL

STOJILJKOVIC I	1995	247	199	MOL GEN GENET
STOJILJKOVIC I	1994	236	531	J MOL BIOL
TAUXE R V	1992		9	CAMPYLOBACTER JEJUNI
THOMAS C E	1994	11	725	MOL MICROBIOL
THOMAS C E	1996	178	4224	J BACTERIOL
TOLMASKY M E	1994	176	213	J BACTERIOL
TOMB J F	1997	388	539	NATURE
TOUATI D	1995	177	2305	J BACTERIOL
TSOLIS R M	1995	177	4628	J BACTERIOL
VANVLIET A H M				UNPUB
VANVLIET A H M	1998	27	405	METHOD MICROBIOL
VENTURI V	1995	17	603	MOL MICROBIOL
VENTURI V	1995	15	1081	MOL MICROBIOL
WASSENAAR T M	1993	132	131	GENE
WERTHEIMER A M	1994	176	5116	J BACTERIOL
WOOLDRIDGE K G	1993	12	325	FEMS MICROBIOL REV
WOOLDRIDGE K G	1994	176	5852	J BACTERIOL
WREN B W	1994	16	994	BIOTECHNIQUES
YAO R J	1993	130	127	GENE

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ACCESSION NUMBER: 1996:522154 SCISEARCH Full-text

THE GENUINE ARTICLE: UW795

TITLE: Isolation and analysis of a fur mutant of  
Neisseria gonorrhoeae

AUTHOR: Thomas C E (Reprint); Sparling P F

CORPORATE SOURCE: UNIV N CAROLINA, SCH MED, DEPT MICROBIOL & IMMUNOL, CHAPEL  
HILL, NC 27599; UNIV N CAROLINA, SCH MED, DEPT MED, CHAPEL  
HILL, NC 27599

COUNTRY OF AUTHOR: USA

SOURCE: JOURNAL OF BACTERIOLOGY, (JUL 1996) Vol. 178, No. 14, pp.  
4224-4232.  
ISSN: 0021-9193.

PUBLISHER: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC  
20036-2904 USA.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 77

ENTRY DATE: Entered STN: 1996

Last Updated on STN: 1996

#### ABSTRACT:

The pathogenic *Neisseria* spp. produce a number of iron-regulated gene products that are thought to be important in virulence. Iron-responsive regulation of these gene products has been attributed to the presence in *Neisseria* spp. of the Fur (ferric uptake regulation) protein. Evidence for the role of Fur in neisserial iron regulation has been indirect because of the inability to make fur null mutations. To circumvent this problem, we used manganese selection to isolate missense \*\*\*mutations\*\*\* of *Neisseria gonorrhoeae* fur. We show that a \*\*\*mutation\*\*\* in gonococcal fur resulted in reduced modulation of expression of four well-stained iron-repressed genes and affected the iron regulation of a broad range of other genes as judged by two-dimensional polyacrylamide gel electrophoresis (PAGE). All 15 of the iron-repressed spots observed by two-dimensional PAGE were at least partially derepressed in the fur \*\*\*mutant\*\*\*, and 17 of the 45 iron-induced spots were affected by the fur \*\*\*mutation\*\*\*. Thus, Fur plays a central role in regulation of iron-repressed gonococcal genes and appears to be involved in regulation of many iron-induced genes. The size and complexity of the iron regulons in *N. gonorrhoeae* are much greater than previously recognized.

CATEGORY: MICROBIOLOGY  
 SUPPL. TERM PLUS: UPTAKE REGULATION PROTEIN; OUTER-  
 MEMBRANE PROTEIN; VIBRIO-CHOLERAЕ; DNA FRAGMENT;  
 TRANSFERRIN UTILIZATION; SALMONELLA-TYPHIMURIUM;  
 IRON ASSIMILATION; GENE-EXPRESSION; UPTAKE SYSTEMS;  
 CLONING

## REFERENCE(S) :

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
ACHTMAN M	1988	168	507	J EXP MED
ANDERSON J E	1994	176	3162	J BACTERIOL
BAGG A	1985	161	450	J BACTERIOL
BAGG A	1987	51	509	MICROBIOL REV
BEALL B W	1995	30	223	CURR MICROBIOL
BERISH S A	1993	61	4599	INFECT IMMUN
BEUCHER M	1995	177	2041	J BACTERIOL
BIEGLE S				IN PRESS GENE
BISWAS G D	1995	63	2958	INFECT IMMUN
BISWAS G D	1977	129	983	J BACTERIOL
BISWAS G D	1989	171	657	J BACTERIOL
BLACK J R	1986	54	710	INFECT IMMUN
BLANTON K J	1990	172	5225	J BACTERIOL
BRIAT J F	1992	138	2475	J GEN MICROBIOL
BRICKMAN T J	1995	177	268	J BACTERIOL
BULLEN J J	1978	80	1	CURR TOP MICROBIOL I
CAMPBELL L A	1979	140	1109	J BACTERIOL
CARBONETTI N	1990	4	1009	MOL MICROBIOL
CATLIN B W	1973	128	178	J INFECT DIS
CHANG A C Y	1978	134	1141	J BACTERIOL
CHEN C Y	1993	10	311	MOL MICROBIOL
CORNELISSEN C N	1992	174	5788	J BACTERIOL
COY M	1991	30	8201	BIOCHEMISTRY-US
ELKINS C	1991	173	391	J BACTERIOL
ELKINS C	1992	6	2617	MOL MICROBIOL
ERNST J F	1978	135	928	J BACTERIOL
FLITTER W	1983	158	310	FEBS LETT
FOSTER J W	1992	174	4317	J BACTERIOL
GOODMAN S D	1991	173	5921	J BACTERIOL
HANTKE K	1981	182	288	MOL GEN GENET
HANTKE K	1987	210	135	MOL GEN GENET
HASSETT D J	1990	172	7293	J BACTERIOL
HEINE R P	1996	174	659	AM J OBSTET GYNECOL
HENNECKE H	1990	4	1621	MOL MICROBIOL
HICKEY E K	1994	143	117	GENE
KELLOGG D S	1963	85	1274	J BACTERIOL
KREUZER K	1975	81	459	GENETICS
LAEMMLI U K	1970	227	680	NATURE
LAM M S	1994	176	5108	J BACTERIOL
LITWIN C M	1993	6	137	CLIN MICROBIOL REV
LITWIN C M	1992	174	1897	J BACTERIOL
LITWIN C M	1993	175	706	J BACTERIOL
LITWIN C M	1994	176	240	J BACTERIOL
MICKELSEN P A	1981	33	555	INFECT IMMUN
MIETZNER T A	1986	51	60	INFECT IMMUN
MILDVAN A S	1979	6	219	CRC CRIT R BIOCHEM
MILLER J H	1972			EXPT MOL GENETICS
MORSE S A	1990		458	NEISSERIAE 1990
NEILANDS J B	1981	50	715	ANN REV BIOCH
NORQVIST A	1978	4	281	FEMS MICROBIOL LETT

OFARRELL P H	1975	250	4007	J BIOL CHEM
PRENTKI P	1984	29	303	GENE
PRINCE R W	1993	175	2589	J BACTERIOL
SAITO T	1991	197	39	EUR J BIOCHEM
SAITO T	1991	197	43	EUR J BIOCHEM
SAMBROOK J	1989			MOL CLONING LAB MANU
SARUBBI F A	1974	120	1284	J BACTERIOL
SCHAFFER S	1985	200	110	MOL GEN GENET
SCHMITT M P	1988	170	5579	J BACTERIOL
STAGGS T M	1991	173	417	J BACTERIOL
STAGGS T M	1994	176	7614	J BACTERIOL
STAGGS T M	1992	6	2507	MOL MICROBIOL
STERN A	1984	37	447	CELL
STOJILJKOVIC I	1995	15	531	MOL MICROBIOL
THOMAS C E	1994	11	725	MOL MICROBIOL
TOLMASKY M E	1994	176	213	J BACTERIOL
TOUATI D	1995	177	2305	J BACTERIOL
TOWBIN H	1979	76	4350	P NATL ACAD SCI USA
TREES D				UNPUB
VENTURI V	1995	15	1081	MOL MICROBIOL
WEE S	1988	1	62	BIOL METALS
WEI Y				UNPUB KLEBSIELLA PNE
WEINBERG E D	1984	64	65	PHYSIOL REV
WERTHEIMER A M	1994	176	5116	J BACTERIOL
WEST S E H	1985	47	388	INFECT IMMUN
WEST S E H	1987	169	3414	J BACTERIOL
WOOLDRIDGE K G	1994	176	5852	J BACTERIOL

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ACCESSION NUMBER: 1993:675386 SCISEARCH Full-text  
 THE GENUINE ARTICLE: ME617  
 TITLE: IDENTIFICATION AND CLONING OF A FUR HOMOLOG FROM  
 NEISSERIA-GONORRHOEAE  
 AUTHOR: BERISH S A (Reprint); SUBBARAO S; CHEN C Y; TREES D L;  
 MORSE S A  
 CORPORATE SOURCE: CTR DIS CONTROL & PREVENT, NATL CTR INFECT DIS, DIV  
 SEXUALLY TRANSMITTED DIS, RES LAB, ATLANTA, GA 30333  
 COUNTRY OF AUTHOR: USA  
 SOURCE: INFECTION AND IMMUNITY, (NOV 1993) Vol. 61, No. 11, pp.  
 4599-4606.  
 ISSN: 0019-9567.  
 PUBLISHER: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC  
 20036-2904 USA.  
 DOCUMENT TYPE: Article; Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 51  
 ENTRY DATE: Entered STN: 1994  
 Last Updated on STN: 1994

# ABSTRACT:

The promoter region of the major iron-regulated protein of *Neisseria gonorrhoeae*, Fbp, has two regions that exhibit homology with the *Escherichia coli* consensus Fur-binding sequences. Gel retardation assays suggested that purified *E. coli* Fur bound to two sites within the Fbp promoter. The presence of a gonococcal Fur homolog was suggested by Southern hybridization under conditions of low stringency, which revealed a DNA locus that exhibited homology to the *E. coli fur* gene. Oligonucleotides derived from the conserved regions of *fur* genes of extremely diverse bacteria were used to amplify a 140-bp fragment of a putative gonococcal *fur* gene. This fragment was used to identify

clones containing the entire gonococcal fur gene. After sequencing the gonococcal fur gene and its promoter region, we found that gonococcal Fur exhibited 50% identity with E. coli Fur at the amino acid level; however, it complemented two E. coli Fur- mutants. The presence of a Fur homolog in N. gonorrhoeae suggests that Fur-regulated genes are widely distributed among extremely diverse bacteria.

CATEGORY: IMMUNOLOGY; INFECTIOUS DISEASES  
 SUPPL. TERM PLUS: IRON-REGULATED PROTEIN; OUTER-MEMBRANE  
 PROTEIN; ESCHERICHIA-COLI; SALMONELLA  
 -TYPHIMURIUM; MOLECULAR-CLONING; STRUCTURAL GENE;  
 TRANSFERRIN; DNA; LACTOFERRIN; EXPRESSION

## REFERENCE(S):

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
AUSUBEL, F M	1987	2		CURRENT PROTOCOLS MO
BAGG, A	1987	51	509	MICROBIOL REV
BERISH, S A	1990	171	1535	J EXP MED
BIRNBOIM, H C	1979	7	1513	NUCLEIC ACIDS RES
BULLEN, J J	1978	80	1	CURR TOP MICROBIOL I
CARBONETTI, N H	1987	84	9084	P NATL ACAD SCI USA
CHEN, J C R	1991	5	1531	MOL MICROBIOL
CORNELISSEN, C N	1992	174	5788	J BACTERIOL
COULTON, J W	1986	165	181	J BACTERIOL
COY, M	1991	30	8201	BIOCHEMISTRY-US
DELCARDAYRE, S	1991		387	IRON BIOMINERALS
DELORENZO, V	1988	173	537	EUR J BIOCHEM
DELORENZO, V	1987	169	2624	J BACTERIOL
DELORENZO, V	1988	203	875	J MOL BIOL
ERNST, J F	1978	135	928	J BACTERIOL
FOSTER, J W	1992	174	4317	J BACTERIOL
GRUNSTEIN, M	1975	72	3961	P NATL ACAD SCI USA
HANTKE, K				COMMUNICATION
HANTKE, K	1984	197	337	MOL GEN GENET
HANTKE, K	1987	210	135	MOL GEN GENET
HENNECKE, H	1990	4	1621	MOL MICROBIOL
LAEMMLI, U K	1970	227	680	NATURE
LITWIN, C M	1992	174	1897	J BACTERIOL
LITWIN, C M	1993	175	706	J BACTERIOL
MANIATIS, T	1982			MOL CLONING
MARMUR, J	1961	3	208	J MOL BIOL
MCKENNA, W R	1988	56	785	INFECT IMMUN
MICKELSEN, P A	1981	33	555	INFECT IMMUN
MICKELSEN, P A	1982	35	915	INFECT IMMUN
MIETZNER, T A	1984	45	410	INFECT IMMUN
MIETZNER, T A	1986	51	60	INFECT IMMUN
MILLER, J H	1972			EXPT MOL GENETICS
MORNA, C P	1990		267	MOL BIOL METHODS BAC
MORSE, S A	1989		639	INFECT DIS
MORSE, S A	1991		453	NEISSERIAE 1990
MORSE, S A	1988	10	S306	REV INFECT DIS S2
PRENTKI, P	1984	29	303	GENE
RPINCE, R W	1993	175	2589	J BACTERIOL
SCHAFFER, S	1985	200	110	MOL GEN GENET
SCHRYVERS, A B	1989	35	409	CAN J MICROBIOL
SHYAMALA, V	1989	84	1	GENE
SOUTHERN, E M	1975	98	503	J MOL BIOL
STAGGS, T M	1991	173	417	J BACTERIOL
STAGGS, T M	1992	6	2507	MOL MICROBIOL
THOMAS, C				COMMUNICATION



THOMPSON, S A	1993	175	811	J BACTERIOL
TSAI, W M	1989	57	2653	INFECT IMMUN
WEINBERG, E D	1978	42	45	MICROBIOL REV
WEST, S E H	1989	2	S92	CLIN MICCROBIOL RE S
WINSHIP, P R	1989	17	1266	NUCLEIC ACIDS RES
YANCEY, R J	1981	32	592	INFECT IMMUN

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ACCESSION NUMBER: 1993:76561 SCISEARCH Full-text

THE GENUINE ARTICLE: KJ722

TITLE: CLONING AND GENETIC-ANALYSIS OF THE VIBRIO-VULNIFICUS-  
FUR GENE AND CONSTRUCTION OF A FUR  
MUTANT BY INVIVO MARKER EXCHANGE

AUTHOR: LITWIN C M (Reprint)

CORPORATE SOURCE: MASSACHUSETTS GEN HOSP, INFECT DIS UNIT, BOSTON, MA 02114  
(Reprint)

AUTHOR: CALDERWOOD S B

CORPORATE SOURCE: HARVARD UNIV, SCH MED, DEPT MICROBIOL & MOLEC GENET,  
BOSTON, MA 02115

COUNTRY OF AUTHOR: USA

SOURCE: JOURNAL OF BACTERIOLOGY, (FEB 1993) Vol. 175, No. 3, pp.  
706-715.

ISSN: 0021-9193.

PUBLISHER: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW,  
WASHINGTON, DC 20005-4171.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: English

REFERENCE COUNT: 65

ENTRY DATE: Entered STN: 1994

Last Updated on STN: 1994

#### ABSTRACT:

*Vibrio vulnificus* infections have been associated with iron overload and preexisting liver disease. Iron may play a major role in the pathogenesis of *V. vulnificus* infections. Many virulence genes, as well as genes involved in the transport of iron by bacteria, are regulated by iron, with increased expression under low-iron conditions. In *Escherichia coli* and *Vibrio cholerae*, transcriptional regulation by iron depends on the *fur*

\*\*\*gene\*\*\* We utilized Southern hybridization under low- and high-stringency conditions with both *E. coli* and *V. cholerae fur*

\*\*\*gene\*\*\* probes to demonstrate that there are *fur*-homologous sequences in the DNAs of *V. vulnificus*, *Vibrio fischeri*, and *Aeromonas sp.* but not in the DNAs of the other bacterial species tested. We developed a restriction map and cloned the *fur*-homologous sequence from *V. vulnificus*. The hybridizing clone of *V. vulnificus* chromosomal DNA complemented a *V. cholerae fur*

\*\*\*mutant\*\*\* DNA sequence analysis confirmed the presence of a 149-amino-acid open reading frame that was 77% homologous to *E. coli Fur* and 93% homologous to *V. cholerae Fur*. Primer extension localized a single promoter for the *V. vulnificus fur* gene. Northern (RNA)

blot analysis and beta-galactosidase assays of an operon fusion to *lacZ* suggested that there was not significant regulation of transcription of *V. vulnificus fur* by iron or the *E. coli Fur* protein. We used marker exchange to construct a *V. vulnificus fur* deletion mutant and confirmed its phenotype by observing overexpression of iron-regulated outer

\*\*\*membrane\*\*\* proteins on sodium dodecyl sulfate-polyacrylamide gel electrophoresis. The *fur* deletion mutant of *V. vulnificus* will be helpful in future studies of the role of iron in *V. vulnificus* pathogenesis.

CATEGORY: MICROBIOLOGY

SUPPL. TERM PLUS: CYTOTOXIN-HEMOLYSIN GENE; IRON UPTAKE SYSTEM;

ESCHERICHIA-COLI; NUCLEOTIDE-SEQUENCE; REGULATORY GENE;  
 CONSTITUTIVE EXPRESSION; SALMONELLA-TYPHIMURIUM;  
 ELASTOLYTIC PROTEASE; SUICIDE VECTOR; VIRULENCE

## REFERENCE(S) :

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
=====	+	+	+	=====
ACTIS, L A	1985	161	736	J BACTERIOL
BIRNBOIM, H C	1979	7	1513	NUCLEIC ACIDS RES
BLAKE, P A	1979	300	1	NEW ENGL J MED
BLOMFELD, I C	1991	5	1447	MOL MICROBIOL
BOYD, J	1990	87	5968	P NATL ACAD SCI USA
BULLEN, J J	1981	3	1127	REV INFECT DIS
CALDERWOOD, S B	1987	169	4759	J BACTERIOL
CALDERWOOD, S B	1988	170	1015	J BACTERIOL
DEGRANDIS, S	1987	169	4313	J BACTERIOL
DELORENZO, V	1988	173	537	EUR J BIOCHEM
DELORENZO, V	1987	169	2624	J BACTERIOL
DONNENBERG, M S	1991	59	4310	INFECT IMMUN
DUNLAP, P V	1992	157	235	ARCH MICROBIOL
DUNLAP, P V	1989	171	1199	J BACTERIOL
DUNLAP, P V	1992	7	203	J BIOLUMIN CHEMILUMI
ERNST, J F	1978	135	928	J BACTERIOL
FARRELL, D H	1990	86	45	GENE
GOLDBERG, M B	1990	58	55	INFECT IMMUN
GOLDBERG, M B	1991	88	1125	P NATL ACAD SCI USA
GRAY, L D	1985	48	62	INFECT IMMUN
GRAY, L D	1987	155	236	J INFECT DIS
HANAHAN, D	1983	166	557	J MOL BIOL
HANTKE, K	1981	182	288	MOL GEN GENET
HAYGOOD, M G	1985	162	209	J BACTERIOL
JOHNSON, D E	1984	150	413	J INFECT DIS
KLONTZ, K C	1988	109	318	ANN INTERN MED
KOTHARY, M H	1985	50	534	INFECT IMMUN
KOTHARY, M H	1987	133	1783	J GEN MICROBIOL
KREGER, A	1981	33	583	INFECT IMMUN
KREGER, A	1981	144	244	J INFECT DIS
KREGER, A S	1984	45	537	INFECT IMMUN
LITWIN, C M				IN PRESS CLIN MICROB
LITWIN, C M	1992	174	1897	J BACTERIOL
MEKALANOS, J J	1983	306	551	NATURE
MICHAELIS, S	1983	154	366	J BACTERIOL
MILLER, J H	1972			EXPT MOL GENETICS
MILLER, S I	1990	172	2485	J BACTERIOL
MILLER, S I	1986	14	7341	NUCLEIC ACIDS RES
MILLER, S I	1989	86	5054	P NATL ACAD SCI USA
MILLER, V L	1988	170	2575	J BACTERIOL
MORRIS, J G	1988	109	261	ANN INTERN MED
MORRIS, J G	1987	53	193	APPL ENVIRON MICROB
MORRIS, J G	1987	40	55	FEMS MICROBIOL LETT
MORRIS, J G	1985	312	343	NEW ENGL J MED
NEALSON, K H	1979	4	105	TRENDS BIOCHEM SCI
PEARSON, W R	1988	85	2444	P NATL ACAD SCI USA
POOLE, K	1988	56	2967	INFECT IMMUN
PRINCE, R W	1991	5	2823	MOL MICROBIOL
RUBY, E G	1976	151	574	BIOL BULL
SALINAS, P C	1989	86	3529	P NATL ACAD SCI USA
SAMBROOK, J	1989			MOL CLONING LABORATO
SANGER, F	1977	74	5463	P NATL ACAD SCI USA
SCHAFFER, S	1985	200	110	MOL GEN GENET

SIMPSON, L M	1987	15	155	CURR MICROBIOL
SIMPSON, L M	1983	42	644	INFECT IMMUN
SIMPSON, L M	1987	55	269	INFECT IMMUN
SOUTHERN, E M	1975	98	503	J MOL BIOL
STAGGS, T M	1991	173	417	J BACTERIOL
STASKAWICZ, B	1987	169	5789	J BACTERIOL
SWARTZMAN, E	1990	172	6797	J BACTERIOL
TESTA, J	1984	45	458	INFECT IMMUN
WRIGHT, A C	1981	34	503	INFECT IMMUN
WRIGHT, A C	1985	50	922	INFECT IMMUN
WRIGHT, A C	1990	58	1769	INFECT IMMUN
YOSHIDA, S I	1985	47	446	INFECT IMMUN

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ACCESSION NUMBER: 2006197277 EMBASE Full-text  
 TITLE: Identification of Salmonella enterica serovar Typhimurium genes important for survival in the swine gastric environment.  
 AUTHOR: Bearson, Shawn M. D. (correspondence); Rasmussen, Mark A.  
 CORPORATE SOURCE: Pre-harvest Food Safety and Enteric Diseases Research Unit, National Animal Disease Center, Ames, IA 50010, United States. sbearson@nadc.ars.usda.gov  
 AUTHOR: Bearson, Bradley L.  
 CORPORATE SOURCE: Swine Odor and Manure Management Research Unit, National Soil Tilth Laboratory, Ames, IA 50010, United States.  
 AUTHOR: Bearson, Shawn M. D. (correspondence)  
 CORPORATE SOURCE: USDA, ARS, NADC, 2300 Dayton Ave., Ames, IA 50014, United States. sbearson@nadc.ars.usda.gov  
 SOURCE: Applied and Environmental Microbiology, (Apr 2006) Vol. 72, No. 4, pp. 2829-2836.  
 Refs: 46  
 ISSN: 0099-2240 CODEN: AEMIDF  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 004 Microbiology: Bacteriology, Mycology, Parasitology and Virology  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 23 May 2006  
 Last Updated on STN: 23 May 2006

ABSTRACT: Since the stomach is a first line of defense for the host against ingested microorganisms, an ex vivo swine stomach contents (SSC) assay was developed to search for genes important for Salmonella enterica serovar Typhimurium survival in the hostile gastric environment. Initial characterization of the SSC assay (pH 3.87) using previously identified, acid-sensitive serovar Typhimurium mutants revealed a 10-fold decrease in survival for a phoP mutant following 20 min of challenge and no survival for mutants oirpoS or fur. To identify additional genes, a signature-tagged mutagenesis bank was constructed and screened in the SSC assay. Nineteen mutants were identified and individually analyzed in the SSC and acid tolerance response assays; 13 mutants exhibited a 10-fold or greater sensitivity in the SSC assay compared to the wild-type strain, but only 3 mutants displayed a 10-fold or greater decrease in survival following pH 3.0 acidic challenge. Further examination determined that the lethal effects of the SSC are pH dependent but that low pH is not the sole killing mechanism(s). Gas chromatography analysis of the SSC revealed lactic acid levels of 126 mM. Upon investigating the effects of lactic acid on serovar Typhimurium survival in a synthetic gastric fluid, not only was a concentration- and time-dependent lethal effect observed, but the phoP, rpoS, fur, and pnp genes were identified

as involved in protection against lactic acid exposure. These studies indicate a role in gastric survival for several serovar Typhimurium genes and imply that the stomach environment is defined by more than low pH.

CONTROLLED TERM: Medical Descriptors:  
 article  
 bacterial gene  
 bacterial infection: ET, etiology  
 bacterium mutant  
 colony forming unit  
     fur gene  
 gas chromatography  
 \*gastroenteritis: ET, etiology  
 gastrointestinal infection: ET, etiology  
 genotype  
 nonhuman  
 nucleotide sequence  
 phoP gene  
 pnp gene  
 polymerase chain reaction  
 rpoS gene  
     \*Salmonella enterica  
     \*Salmonella typhimurium  
 stomach juice  
 stomach pH  
 survival

CONTROLLED TERM: Drug Descriptors:  
 lactic acid

CAS REGISTRY NO.: (lactic acid) 113-21-3, 50-21-5

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ACCESSION NUMBER: 1992007009 EMBASE Full-text  
 TITLE: Regulation of toxA and regA by the Escherichia coli fur gene and identification of a Fur homologue in Pseudomonas aeruginosa PA103 and PA01.  
 AUTHOR: Prince, P.W.; Storey, D.G.; Vasil, A.I.; Vasil, M.L. (correspondence)  
 CORPORATE SOURCE: Dept. Microbiol./Immunology, University of Colorado, Health Science Center, Denver, CO 80262, United States.  
 SOURCE: Molecular Microbiology, (1991) Vol. 5, No. 11, pp. 2823-2831.  
 ISSN: 0950-382X CODEN: MOMIEE  
 COUNTRY: United Kingdom  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 004 Microbiology: Bacteriology, Mycology, Parasitology and Virology  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 20 Mar 1992  
 Last Updated on STN: 20 Mar 1992

ABSTRACT: A multicopy plasmid containing the Escherichia coli fur \*\*\*gene\*\*\* was introduced into Pseudomonas aeruginosa strain PA103C. This strain contains a toxA-lacZ fusion integrated into its chromosome at the toxA locus. Beta-galactosidase synthesis in this strain is regulated by iron, as is seen for exotoxin A production. Beta-galactosidase synthesis and exotoxin A production in PA103 containing multiple copies of E. coli fur was still repressed in low iron conditions. The transcription of regA, a positive regulator of toxA, was also found to be inhibited by multiple copies of the E. coli fur gene. In addition, the ability of PA103C

containing multiple copies of *E. coli* fur to produce protease was greatly reduced relative to PA103C containing a vector control. A polyclonal rabbit serum containing antibodies that recognize *E. coli* Fur was used to screen whole-cell extracts from *Vibrio cholerae*, *Shigella flexneri*, *Salmonella typhimurium* and *Pseudomonas aeruginosa*. All strains tested expressed a protein that was specifically recognized by the anti-Fur serum. These results and those described above suggest that Fur structure and function are conserved in a variety of distinct bacterial genera and that at least some of these different genera use this regulatory protein to control genes encoding virulence factors.

CONTROLLED TERM: Medical Descriptors:  
 article  
 \*escherichia coli  
 gene control  
 nonhuman  
 priority journal  
 \*pseudomonas aeruginosa  
   salmonella typhimurium  
 \*sequence homology  
 shigella flexneri  
 vibrio cholerae

CONTROLLED TERM: Drug Descriptors:  
 beta galactosidase: EC, endogenous compound  
 exotoxin a: TO, drug toxicity  
 exotoxin a: EC, endogenous compound  
 proteinase: EC, endogenous compound  
 unclassified drug

CAS REGISTRY NO.: (proteinase) 9001-92-7

## TEXT SEARCH PART 2

=> fil pascal biotechno wpix biosis dissabs lifesci esbio biotechds bioeng  
scisearch

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=> d que l117; d que l124

L107 83 SEA PFUR? OR DELTAPFUR?

L108 4 SEA TTARA?

L117 0 SEA L107 AND L108

L99 249856 SEA SALMONELLA

L105 965 SEA MANNOSE(1A) PHOSPHATE ISOMERASE

L106 5259 SEA PMI OR ΔPMI OR DELTAPMI

L110 2667600 SEA MUTAT? OR MUTANT#

L120 100416 SEA L99(W) TYPHIMURIUM

L121 34 SEA (L105 OR L106) AND L110 AND L120

L123 13465 SEA L110(S)((L106 OR L105 OR L120))

L124 31 SEA L121 AND L123

=> s l124 not l129,l126

L134 21 L124 NOT (L129 OR L126)

L129,L126 WERE PREVIOUSLY PRINTED

=> fil capl; d que l24; d que l23; d que l33

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FILE COVERS 1907 - 30 Nov 2010 VOL 153 ISS 23  
 FILE LAST UPDATED: 29 Nov 2010 (20101129/ED)  
 REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2010  
 USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2010

Caplus now includes complete International Patent Classification (IPC) reclassification data for the fourth quarter of 2010.

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L24 0 SEA FILE=CAPLUS SPE=ON ABB=ON TTARACP?/BI

L23 3 SEA FILE=CAPLUS SPE=ON ABB=ON PFUR/BI

L3 37998 SEA FILE=CAPLUS SPE=ON ABB=ON SALMONELLA/CW  
 L7 51696 SEA FILE=CAPLUS SPE=ON ABB=ON ATTENUAT?/OBI  
 L22 970 SEA FILE=CAPLUS SPE=ON ABB=ON PMI/BI  
 L28 328337 SEA FILE=CAPLUS SPE=ON ABB=ON MUTAT?/OBI OR MUTANT#/OBI  
 L29 18181 SEA FILE=CAPLUS SPE=ON ABB=ON L3(L) TYPHIMURIUM/OBI  
 L31 10 SEA FILE=CAPLUS SPE=ON ABB=ON L22 AND L28 AND L29  
 L32 9 SEA FILE=CAPLUS SPE=ON ABB=ON L22 AND L28 AND L29 AND L7  
 L33 1 SEA FILE=CAPLUS SPE=ON ABB=ON L31 NOT L32

=> s 123,133 not 1130,135

L135 4 (L23 OR L33) NOT (L130 OR L35) L130,L35 WERE PREVIOUSLY  
 PRINTED

=> fil embase; d que 191; d que 192; d que 193; d que 195; d que 196

FILE 'EMBASE' ENTERED AT 10:26:36 ON 30 NOV 2010

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FILE COVERAGE: EMBASE-originated material 1947 to 30 Nov 2010 (20101130/ED)  
Unique MEDLINE content 1948 to present

EMBASE is now updated daily. SDI frequency remains weekly (default)  
and biweekly.

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

For further assistance, please contact your local helpdesk.

```

L77      3 SEA FILE=EMBASE SPE=ON  ABB=ON  TTARA?
L83      25 SEA FILE=EMBASE SPE=ON  ABB=ON  PFUR?
L91      0 SEA FILE=EMBASE SPE=ON  ABB=ON  L77 AND L83

L68      67092 SEA FILE=EMBASE SPE=ON  ABB=ON  SALMONELLA+NT/CT
L77      3 SEA FILE=EMBASE SPE=ON  ABB=ON  TTARA?
L83      25 SEA FILE=EMBASE SPE=ON  ABB=ON  PFUR?
L92      0 SEA FILE=EMBASE SPE=ON  ABB=ON  L68 AND (L77 OR L83)

L68      67092 SEA FILE=EMBASE SPE=ON  ABB=ON  SALMONELLA+NT/CT
L73      325 SEA FILE=EMBASE SPE=ON  ABB=ON  MANNOSE PHOSPHATE ISOMERASE/CT
L93      5 SEA FILE=EMBASE SPE=ON  ABB=ON  L73 AND L68

L69      25567 SEA FILE=EMBASE SPE=ON  ABB=ON  SALMONELLA TYPHIMURIUM/CT
L75      1095 SEA FILE=EMBASE SPE=ON  ABB=ON  PMI OR ΔPMI OR DELTAPMI
L95      5 SEA FILE=EMBASE SPE=ON  ABB=ON  L69 AND L75

L68      67092 SEA FILE=EMBASE SPE=ON  ABB=ON  SALMONELLA+NT/CT
L75      1095 SEA FILE=EMBASE SPE=ON  ABB=ON  PMI OR ΔPMI OR DELTAPMI
L78      11332 SEA FILE=EMBASE SPE=ON  ABB=ON  LIVE VACCINE/CT
L79      189362 SEA FILE=EMBASE SPE=ON  ABB=ON  ATTENUAT?
L80      544225 SEA FILE=EMBASE SPE=ON  ABB=ON  MUTATION+NT/CT
L81      48065 SEA FILE=EMBASE SPE=ON  ABB=ON  MUTANT/CT OR BACTERIUM
          MUTANT+NT/CT
L82      31722 SEA FILE=EMBASE SPE=ON  ABB=ON  MUTANT PROTEIN/CT
L96      5 SEA FILE=EMBASE SPE=ON  ABB=ON  L75 AND L68 AND (L78 OR L79 OR
          L80 OR L81 OR L82)

```

=> s 193,195,196 not 1131,197

```

L136      11 (L93 OR L95 OR L96) NOT (L131 OR L97)      L131,L97 WERE
                                                         PREVIOUSLY PRINTED

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=> fil medl; d que 146; d que 145; d que 161; d que 162; d que 164

FILE 'MEDLINE' ENTERED AT 10:26:38 ON 30 NOV 2010



FILE LAST UPDATED: 27 Nov 2010 (20101127/UP). FILE COVERS 1946 TO DATE.

MEDLINE and LMEDLINE have been updated with the 2010 Medical Subject Headings (MeSH) vocabulary and tree numbers from the U.S. National Library of Medicine (NLM). Additional information is available at

[http://www.nlm.nih.gov/pubs/techbull/nd09/nd09\\_medline\\_data\\_changes\\_2010.html](http://www.nlm.nih.gov/pubs/techbull/nd09/nd09_medline_data_changes_2010.html).

The Medline file has been reloaded effective January 24, 2010. See HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

See HELP RANGE before carrying out any RANGE search.

```
L46          0 SEA FILE=MEDLINE SPE=ON  ABB=ON  TTARACP?

L45          2 SEA FILE=MEDLINE SPE=ON  ABB=ON  PFUR

L37          48420 SEA FILE=MEDLINE SPE=ON  ABB=ON  SALMONELLA+NT/CT
L59          262 SEA FILE=MEDLINE SPE=ON  ABB=ON  MANNOSE-6-PHOSPHATE ISOMERASE/
CT
L61          5 SEA FILE=MEDLINE SPE=ON  ABB=ON  L59 AND L37

L37          48420 SEA FILE=MEDLINE SPE=ON  ABB=ON  SALMONELLA+NT/CT
L40          7659 SEA FILE=MEDLINE SPE=ON  ABB=ON  VACCINES, ATTENUATED/CT
L41          491950 SEA FILE=MEDLINE SPE=ON  ABB=ON  MUTATION+NT/CT
L42          11848 SEA FILE=MEDLINE SPE=ON  ABB=ON  MUTANT PROTEINS+NT/CT
L44          958 SEA FILE=MEDLINE SPE=ON  ABB=ON  PMI OR ΔPMI
L62          3 SEA FILE=MEDLINE SPE=ON  ABB=ON  L44 AND L37 AND (L40 OR L41
OR L42)

L44          958 SEA FILE=MEDLINE SPE=ON  ABB=ON  PMI OR ΔPMI
L63          22571 SEA FILE=MEDLINE SPE=ON  ABB=ON  SALMONELLA TYPHIMURIUM/CT
L64          4 SEA FILE=MEDLINE SPE=ON  ABB=ON  L63 AND L44
```

=> s 145,161,162,164 not 1132,166

```
L137          10 (L45 OR L61 OR L62 OR L64) NOT (L132 OR L66)      L132,L66 WERE
PREVIOUSLY PRINTED
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=> => dup rem 1137,1135,1134,1136

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PROCESSING COMPLETED FOR L137

PROCESSING COMPLETED FOR L135

PROCESSING COMPLETED FOR L134

PROCESSING COMPLETED FOR L136

L138 25 DUP REM L137 L135 L134 L136 (21 DUPLICATES REMOVED)

ANSWERS '1-10' FROM FILE MEDLINE

ANSWERS '11-12' FROM FILE CAPLUS

ANSWERS '13-15' FROM FILE WPIX

ANSWER '16' FROM FILE BIOSIS

ANSWER '17' FROM FILE DISSABS

ANSWER '18' FROM FILE LIFESCI

ANSWER '19' FROM FILE ESBIOBASE

ANSWER '20' FROM FILE BIOTECHDS

ANSWER '21' FROM FILE SCISEARCH

ANSWERS '22-25' FROM FILE EMBASE

=> d iall 1-10; d ibib abs hitind 11-12; d ifull 13-15; d iall 16-25;fil hom

L138 ANSWER 1 OF 25 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2009453047 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 19564693

TITLE: Structures of mannose-6-phosphate isomerase from Salmonella  
 typhimurium bound to metal atoms and substrate:  
 implications for catalytic mechanism.

AUTHOR: Sagurthi S R; Gowda Giri; Savithri H S; Murthy M R N

CORPORATE SOURCE: Molecular Biophysics Unit, Indian Institute of Science,  
 Bangalore 560 012, India.

SOURCE: Acta crystallographica. Section D, Biological crystallography, (2009 Jul) Vol. 65, No. Pt 7, pp. 724-32. Electronic Publication: 2009-06-20. Journal code: 9305878. E-ISSN: 1399-0047. L-ISSN: 0907-4449.

PUB. COUNTRY: Denmark

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200910

ENTRY DATE: Entered STN: 2 Jul 2009  
Last Updated on STN: 2 Oct 2009  
Entered Medline: 1 Oct 2009

## ABSTRACT:

Mannose-6-phosphate isomerase (MPI) catalyzes the interconversion of mannose 6-phosphate and fructose 6-phosphate. X-ray crystal structures of MPI from *Salmonella typhimurium* in the apo form (with no metal bound) and in the holo form (with bound Zn<sup>2+</sup>) and two other structures with yttrium bound at an inhibitory site and complexed with Zn<sup>2+</sup> and fructose 6-phosphate (F6P) were determined in order to gain insights into the structure and the isomerization mechanism. Isomerization involves acid/base catalysis with proton transfer between the C1 and C2 atoms of the substrate. His99, Lys132, His131 and Asp270 are close to the substrate and are likely to be the residues involved in proton transfer. The interactions observed at the active site suggest that the ring-opening step is probably catalyzed by His99 and Asp270. An active-site loop consisting of residues 130-133 undergoes conformational changes upon substrate binding. Zn<sup>2+</sup> binding induces structural order in the loop consisting of residues 50-54. The metal atom appears to play a role in substrate binding and is probably also important for maintaining the architecture of the active site. Isomerization probably follows the previously suggested cis-enediol mechanism.

CONTROLLED TERM: Amino Acid Sequence  
\*Biocatalysis  
Catalytic Domain  
Crystallography, X-Ray  
Holoenzymes: CH, chemistry  
Holoenzymes: ME, metabolism  
\*Mannose-6-Phosphate Isomerase: CH, chemistry  
Mannose-6-Phosphate Isomerase: ME, metabolism  
Models, Molecular  
Molecular Sequence Data  
Protein Structure, Tertiary  
\*Salmonella typhimurium: EN, enzymology  
Sequence Alignment  
Substrate Specificity  
\*Ytterbium: CH, chemistry  
\*Zinc: CH, chemistry

CAS REGISTRY NO.: 7440-64-4 (Ytterbium); 7440-66-6 (Zinc)

CHEMICAL NAME: 0 (Holoenzymes); EC 5.3.1.8 (Mannose-6-Phosphate Isomerase)

L138 ANSWER 2 OF 25 MEDLINE on STN DUPLICATE 3

ACCESSION NUMBER: 2008101007 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 18259054

TITLE: Cloning, expression, purification, crystallization and preliminary X-ray crystallographic analysis of the mannose 6-phosphate isomerase from *Salmonella typhimurium*.

AUTHOR: Gowda Giri; Sagurthi Someswar Rao; Savithri H S; Murthy M R N

CORPORATE SOURCE: Molecular Biophysics Unit, Indian Institute of Science,

SOURCE: Bangalore 560 012, India.  
 Acta crystallographica. Section F, Structural biology and  
 crystallization communications, (2008 Feb 1) Vol. 64, No.  
 Pt 2, pp. 81-4. Electronic Publication: 2008-01-18.  
 Journal code: 101226117. E-ISSN: 1744-3091. L-ISSN:  
 1744-3091.  
 Report No.: NLM-PMC2374180.  
 PUB. COUNTRY: England: United Kingdom  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200808  
 ENTRY DATE: Entered STN: 9 Feb 2008  
 Last Updated on STN: 8 Aug 2008  
 Entered Medline: 7 Aug 2008

## ABSTRACT:

Mannose 6-phosphate isomerase (MPI; EC 5.3.1.8) catalyzes the reversible isomerization of D-mannose 6-phosphate (M6P) and D-fructose 6-phosphate (F6P). In the eukaryotes and prokaryotes investigated to date, the enzyme has been reported to play a crucial role in D-mannose metabolism and supply of the activated mannose donor guanosine diphosphate D-mannose (GDP-D-mannose). In the present study, MPI was cloned from *Salmonella typhimurium*, overexpressed in *Escherichia coli* and purified using Ni-NTA affinity column chromatography. Purified MPI crystallized in space group P2(1)2(1)2(1), with unit-cell parameters  $a = 36.03$ ,  $b = 92.2$ ,  $c = 111.01$  Å. A data set extending to 1.66 Å resolution was collected with 98.8% completeness using an image-plate detector system mounted on a rotating-anode X-ray generator. The asymmetric unit of the crystal cell was compatible with the presence of a monomer of MPI. A preliminary structure solution of the enzyme has been obtained by molecular replacement using *Candida albicans* MPI as the phasing model and the program Phaser. Further refinement and model building are in progress.

CONTROLLED TERM: Base Sequence  
 Chromatography, Affinity  
 Cloning, Molecular  
 Crystallization  
 Crystallography, X-Ray  
 DNA Primers  
 Electrophoresis, Polyacrylamide Gel  
 \*Mannose-6-Phosphate Isomerase: CH, chemistry  
 Mannose-6-Phosphate Isomerase: GE, genetics  
 Mannose-6-Phosphate Isomerase: IP, isolation &  
 purification  
 Polymerase Chain Reaction  
 \*Salmonella typhimurium: EN, enzymology

CHEMICAL NAME: 0 (DNA Primers); EC 5.3.1.8 (Mannose-6-Phosphate Isomerase)  
 MEDLINE REFERENCE COUNT: 13 There are 13 cited references available in  
 MEDLINE for this document.

## REFERENCE(S): CITED REFERENCES AVAILABLE IN MEDLINE

- (1) Shinabarger, D; J Biol Chem. 1991 Feb 5, V266(4), P2080-8. MEDLINE
- (2) Gracy, R W; J Biol Chem. 1968 Aug 10, V243(15), P4109-16. MEDLINE
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L138 ANSWER 3 OF 25 MEDLINE on STN DUPLICATE 4  
 ACCESSION NUMBER: 2003545311 MEDLINE Full-text  
 DOCUMENT NUMBER: PubMed ID: 14622419  
 TITLE: An anti-repression Fur operator upstream of the promoter is required for iron-mediated transcriptional autoregulation in *Helicobacter pylori*.  
 AUTHOR: Delany Isabel; Spohn Gunther; Rappuoli Rino; Scarlato Vincenzo  
 CORPORATE SOURCE: Biochemistry and Molecular Biology Unit, IRIS, Chiron S rl, Via Fiorentina 1, 53100 Siena, Italy.  
 SOURCE: Molecular microbiology, (2003 Nov) Vol. 50, No. 4, pp. 1329-38.  
 Journal code: 8712028. ISSN: 0950-382X. L-ISSN: 0950-382X.  
 PUB. COUNTRY: England: United Kingdom  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200404  
 ENTRY DATE: Entered STN: 20 Nov 2003  
 Last Updated on STN: 30 Apr 2004  
 Entered Medline: 29 Apr 2004

## ABSTRACT:

The Fur protein acts as a regulator of iron-dependent gene transcription in bacteria. In *Helicobacter pylori*, Fur regulates iron-activated and iron-repressed promoters. It also acts as an autoregulatory rheostat of transcription to fine-tune its own expression in response to iron by binding to three operators at its own promoter *P<sub>Fur</sub>*. Using biochemical and genetic analyses, here we show that the distal upstream operator III (centred at -110) is essential for iron regulation of *P<sub>Fur</sub>* and functions as an anti-repression site that is bound by the iron-free form of Fur to induce transcription. Furthermore, operator I (centred at -50) may have a dual role both as a high-affinity binding site for Fur and as an UP element. We propose that its role is ensuring that Fur expression is not repressed below a minimum threshold level. Our data supports a novel promoter architecture and mechanism of regulation by Fur.

CONTROLLED TERM: \*Bacterial Proteins: GE, genetics  
 Bacterial Proteins: ME, metabolism  
 Base Sequence  
 \*Gene Expression Regulation, Bacterial  
 \*Helicobacter pylori: GE, genetics  
 Helicobacter pylori: ME, metabolism  
 \*Iron: ME, metabolism  
 Models, Genetic  
 Molecular Sequence Data  
 \*Operator Regions, Genetic  
 Promoter Regions, Genetic  
 Recombinant Fusion Proteins: ME, metabolism  
 \*Repressor Proteins: GE, genetics  
 Repressor Proteins: ME, metabolism  
 \*Transcription, Genetic

CAS REGISTRY NO.: 7439-89-6 (Iron)  
 CHEMICAL NAME: 0 (Bacterial Proteins); 0 (Recombinant Fusion Proteins); 0 (Repressor Proteins); 0 (ferric uptake regulating proteins, bacterial)

L138 ANSWER 4 OF 25 MEDLINE on STN DUPLICATE 6  
 ACCESSION NUMBER: 1993127654 MEDLINE Full-text  
 DOCUMENT NUMBER: PubMed ID: 1336259  
 TITLE: Regulation of purine biosynthesis. I. Isolation of add::MudJ (lacZ, Kanr) insertions and genetic mapping.  
 AUTHOR: Wang A; Chen X; Dai X; Tang G  
 CORPORATE SOURCE: Institute of Microbiology, Academia Sinica, Beijing.  
 SOURCE: Wei sheng wu xue bao = Acta microbiologica Sinica, (1992 Oct) Vol. 32, No. 5, pp. 328-33.  
 Journal code: 21610860R. ISSN: 0001-6209. L-ISSN: 0001-6209.  
 PUB. COUNTRY: China  
 DOCUMENT TYPE: (ENGLISH ABSTRACT)  
 Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 LANGUAGE: Chinese  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199302  
 ENTRY DATE: Entered STN: 26 Feb 1993  
 Last Updated on STN: 29 Jan 1999  
 Entered Medline: 11 Feb 1993

## ABSTRACT:

Report here is the isolation of adenosine deaminase deficient mutants and genetic mapping. Engineering transposon MudJ (lacZ, Kanr) was used for mutagenesis and six add::MudJ were obtained among 20,000 Kanr transductants. Adenosine deaminase activity of these mutants were assayed and all are negative. Cotransduction analysis of add::MudJ indicated that add is 70% linked to *pmi*(31') and 37% linked to *zxx1900::Tn10d-tet* insertion which is 10% linked to *purR*(30'). Three points cross showed that add is located between *pmi* and *Tn10d-tet* insertion. Therefore the gene order is *purR-zxx1900::Tn10d-tet-add-pmi*.

CONTROLLED TERM: Adenosine Deaminase: GE, genetics  
 \*Chromosome Mapping  
 \*DNA Transposable Elements  
 Gene Expression Regulation, Bacterial  
 \*Genome, Bacterial  
 \*Purines: ME, metabolism  
 \*Salmonella typhimurium: GE, genetics  
 Transduction, Genetic

CHEMICAL NAME: 0 (DNA Transposable Elements); 0 (Purines); EC 3.5.4.4 (Adenosine Deaminase)

GENE NAME: MudJ

L138 ANSWER 5 OF 25 MEDLINE on STN DUPLICATE 7  
 ACCESSION NUMBER: 1991147185 MEDLINE Full-text  
 DOCUMENT NUMBER: PubMed ID: 1997412  
 TITLE: Mutations at *rfc* or *pmi* attenuate Salmonella typhimurium virulence for mice.  
 AUTHOR: Collins L V; Attridge S; Hackett J  
 CORPORATE SOURCE: Department of Microbiology, University of Adelaide, Australia.  
 SOURCE: Infection and immunity, (1991 Mar) Vol. 59, No. 3, pp. 1079-85.  
 Journal code: 0246127. ISSN: 0019-9567. L-ISSN: 0019-9567.  
 Report No.: NLM-PMC258370.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 LANGUAGE: English

FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199104  
 ENTRY DATE: Entered STN: 19 Apr 1991  
 Last Updated on STN: 6 Feb 1998  
 Entered Medline: 2 Apr 1991

## ABSTRACT:

Insertion mutations were constructed in cloned *pmi* and *rfc* genes of *Salmonella typhimurium*, and these mutations were recombined (singly) into the chromosome of mouse-virulent *S. typhimurium* C5, displacing the wild-type alleles. Phage sensitivity profiles, lipopolysaccharide analysis, and DNA blotting all confirmed that the replacement events had occurred. The mutations were complemented by plasmid-borne wild-type alleles, as judged by the restoration of wild-type phage plaquing profiles and lipopolysaccharide production (both mutants) and the restoration of *pmi*-encoded enzyme production (*pmi* mutant). The virulence, persistence, and immunizing capacities of the mutants fed to mice were compared with those of the wild-type strain and complemented mutants. Both mutants were much reduced in virulence, with the *rfc* mutant being avirulent even at 10(9) bacteria per mouse. This mutant was also avirulent at up to 10(6) bacteria per mouse when administered intraperitoneally. Both the *rfc* and *pmi* mutant strains persisted in the Peyer's patches of the gut after feeding and were capable of colonizing the deeper tissues of the mice from such initial infective foci. Both mutant strains were effective as live oral vaccines (10(7) bacteria or more) against oral *S. typhimurium* challenge (10(4) 50% lethal doses; 6 x 10(8) bacteria) in mice.

CONTROLLED TERM: Check Tags: Female  
 Animals  
 Antibodies, Bacterial: IM, immunology  
 Cloning, Molecular  
 Electrophoresis, Polyacrylamide Gel  
 \*Genes, Bacterial  
 Immunity  
 Mannose-6-Phosphate Isomerase: ME, metabolism  
 Mice  
 Mice, Inbred BALB C  
 \*Mutagenesis, Insertional  
 Peyer's Patches: IM, immunology  
 Plasmids  
 Salmonella Infections, Animal: IM, immunology  
 Salmonella Infections, Animal: MO, mortality  
 Salmonella typhimurium: EN, enzymology  
 Salmonella typhimurium: GE, genetics  
 \*Salmonella typhimurium: PY, pathogenicity  
 Virulence: GE, genetics

CHEMICAL NAME: 0 (Antibodies, Bacterial); EC 5.3.1.8 (Mannose-6-Phosphate Isomerase)

GENE NAME: *pmi*; *rfc*

MEDLINE REFERENCE COUNT: 26 There are 26 cited references available in MEDLINE for this document.

## REFERENCE(S): CITED REFERENCES AVAILABLE IN MEDLINE

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- (3) Lyman, M B; Infect Immun. 1976 Jun, V13(6), P1539-42. MEDLINE
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L138 ANSWER 6 OF 25                      MEDLINE on STN                      DUPLICATE 8

ACCESSION NUMBER: 1991100353                      MEDLINE      Full-text

DOCUMENT NUMBER: PubMed ID: 1987157

TITLE:                      Localization of the terminal steps of O-antigen synthesis  
in Salmonella typhimurium.

AUTHOR:                      McGrath B C; Osborn M J

CORPORATE SOURCE:                      Department of Microbiology, University of Connecticut  
Health Center, Farmington 06030.

CONTRACT NUMBER:                      AI-08650 (United States NIAID NIH HHS)  
GM-42339 (United States NIGMS NIH HHS)

SOURCE:                      Journal of bacteriology, (1991 Jan) Vol. 173, No. 2, pp.  
649-54.  
Journal code: 2985120R. ISSN: 0021-9193. L-ISSN: 0021-9193.  
Report No.: NLM-PMC207056.

PUB. COUNTRY:                      United States

DOCUMENT TYPE:                      Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)

LANGUAGE:                      English

FILE SEGMENT:                      Priority Journals

ENTRY MONTH:                      199102

ENTRY DATE:                      Entered STN: 29 Mar 1991  
Last Updated on STN: 3 Feb 1997  
Entered Medline: 20 Feb 1991

ABSTRACT:

Previous immunoelectron microscopic studies have shown that both the final intermediate in O-antigen synthesis, undecaprenol-linked O polymer, and newly synthesized O-antigenic lipopolysaccharide are localized to the periplasmic face of the inner membrane (C. A. Mulford and M. J. Osborn, Proc. Natl. Acad. Sci. USA 80:1159-1163, 1983). In vivo pulse-chase experiments now provide further evidence that attachment of O antigen to core lipopolysaccharide, as well as polymerization of O-specific polysaccharide chains, takes place at the periplasmic face of the membrane. Mutants doubly conditional in lipopolysaccharide synthesis [kdsA(Ts) *pmi*] were constructed in which synthesis of core lipopolysaccharide and O antigen are temperature sensitive and mannose dependent, respectively. Periplasmic orientation of O antigen:core lipopolysaccharide ligase was established by experiments showing rapid chase of undecaprenol-linked O polymer, previously accumulated at 42 degrees C in the absence of core synthesis, into lipopolysaccharide following resumption of core formation at 30 degrees C. In addition, chase of the monomeric O-specific tetrasaccharide unit into lipopolysaccharide was found in similar experiments in an O-polymerase-negative [rfc kdsA(Ts) *pmi*] mutant, suggesting that polymerization of O chains



also occurs at the external face of the inner membrane.

CONTROLLED TERM: Chromatography, Gel  
Electrophoresis, Polyacrylamide Gel  
Galactose: ME, metabolism  
Kinetics  
Mannose: ME, metabolism  
\*O Antigens  
\*Polyisoprenyl Phosphate Sugars: IP, isolation & purification  
\*Polysaccharides, Bacterial: BI, biosynthesis  
Polysaccharides, Bacterial: IP, isolation & purification  
\*Salmonella typhimurium: IM, immunology  
Salmonella typhimurium: ME, metabolism  
Tritium  
CAS REGISTRY NO.: 10028-17-8 (Tritium); 26566-61-0 (Galactose); 31103-86-3 (Mannose)  
CHEMICAL NAME: 0 (O Antigens); 0 (O-specific polysaccharide, Salmonella); 0 (Polyisoprenyl Phosphate Sugars); 0 (Polysaccharides, Bacterial)  
MEDLINE REFERENCE COUNT: 13 There are 13 cited references available in MEDLINE for this document.

REFERENCE(S): CITED REFERENCES AVAILABLE IN MEDLINE

- (1) Goldman, R C; J Bacteriol. 1990 Sep, V172(9), P5352-9. MEDLINE
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L138 ANSWER 7 OF 25 MEDLINE on STN DUPLICATE 9  
ACCESSION NUMBER: 1991348522 MEDLINE Full-text  
DOCUMENT NUMBER: PubMed ID: 1879695  
TITLE: Sequence of the phosphomannose isomerase-encoding gene of Salmonella typhimurium.  
AUTHOR: Collins L V; Hackett J  
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Adelaide, South Australia.  
SOURCE: Gene, (1991 Jul 15) Vol. 103, No. 1, pp. 135-6.  
Journal code: 7706761. ISSN: 0378-1119. L-ISSN: 0378-1119.  
PUB. COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
OTHER SOURCE: GENBANK-M64053; GENBANK-M64054; GENBANK-M64055;  
GENBANK-M64056; GENBANK-M64057; GENBANK-M64058;  
GENBANK-M64059; GENBANK-M64060; GENBANK-S53120;  
GENBANK-X57117  
ENTRY MONTH: 199110  
ENTRY DATE: Entered STN: 20 Oct 1991  
Last Updated on STN: 6 Feb 1998  
Entered Medline: 3 Oct 1991

## ABSTRACT:

The *pmi* gene, encoding phosphomannose isomerase, of *Salmonella typhimurium*, was cloned in *Escherichia coli* K-12, and the protein product visualised in minicells. The cloned gene was sequenced; there was 77.4% nucleotide homology between the cloned *pmi* gene and the analogous *manA* gene of *E. coli* K-12, and 86.2% amino acid sequence homology between their presumptive gene products.

CONTROLLED TERM: Amino Acid Sequence  
Base Sequence  
Cloning, Molecular  
*Escherichia coli*: ME, metabolism  
\*Mannose-6-Phosphate Isomerase: GE, genetics  
Molecular Sequence Data  
Open Reading Frames: GE, genetics  
\**Salmonella typhimurium*: EN, enzymology  
*Salmonella typhimurium*: GE, genetics  
Sequence Homology, Nucleic Acid  
CHEMICAL NAME: EC 5.3.1.8 (Mannose-6-Phosphate Isomerase)  
GENE NAME: *pmi*

L138 ANSWER 8 OF 25 MEDLINE on STN  
ACCESSION NUMBER: 2008567832 MEDLINE Full-text  
DOCUMENT NUMBER: PubMed ID: 18756754  
TITLE: Ecological stress and biological rhythms (on Materials of the International Congress "The health and education in XXI century". Conceptions of civilization diseases. *PFUR*, 2007).  
AUTHOR: Frolov V A; Rapoport S I; Chibisov S M; Halberg F  
SOURCE: *Klinicheskaja meditsina*, (2008) Vol. 86, No. 7, pp. 73-4.  
Journal code: 2985204R. ISSN: 0023-2149. L-ISSN: 0023-2149.  
PUB. COUNTRY: Russia (Federation)  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: Russian  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200811  
ENTRY DATE: Entered STN: 2 Sep 2008  
Last Updated on STN: 19 Nov 2008  
Entered Medline: 18 Nov 2008  
CONTROLLED TERM: \*Circadian Rhythm: PH, physiology  
\*Congresses as Topic  
\*Environmental Exposure: AE, adverse effects  
\*Environmental Health  
\*Environmental Illness  
Environmental Illness: EP, epidemiology  
Environmental Illness: ET, etiology  
Environmental Illness: PP, physiopathology  
Humans  
World Health

L138 ANSWER 9 OF 25 MEDLINE on STN  
ACCESSION NUMBER: 2001526253 MEDLINE Full-text  
DOCUMENT NUMBER: PubMed ID: 11238967  
TITLE: Molecular evolution of the GDP-mannose pathway genes (*manB* and *manC*) in *Salmonella enterica*.  
AUTHOR: Jensen S O; Reeves P R  
CORPORATE SOURCE: Department of Microbiology (G08), University of Sydney, New South Wales 2006, Australia.  
SOURCE: *Microbiology* (Reading, England), (2001 Mar) Vol. 147, No. Pt 3, pp. 599-610.  
Journal code: 9430468. ISSN: 1350-0872. L-ISSN: 1350-0872.

PUB. COUNTRY: England: United Kingdom  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 OTHER SOURCE: GENBANK-AY012160; GENBANK-AY012161; GENBANK-AY012162;  
 GENBANK-AY012163; GENBANK-AY012164; GENBANK-AY012165;  
 GENBANK-AY012166; GENBANK-AY012167; GENBANK-AY012168;  
 GENBANK-AY012169; GENBANK-AY012170; GENBANK-AY012171;  
 GENBANK-AY012172; GENBANK-AY012173; GENBANK-AY012174;  
 GENBANK-AY012175; GENBANK-AY012176; GENBANK-AY012177;  
 GENBANK-AY012178; GENBANK-AY012179; GENBANK-AY012180;  
 GENBANK-AY012181; GENBANK-AY012182; GENBANK-AY012183;  
 GENBANK-AY012184; GENBANK-AY012185; GENBANK-AY012186;  
 GENBANK-AY012187; GENBANK-AY012188; GENBANK-AY012189;  
 GENBANK-AY012190; GENBANK-AY012191; GENBANK-AY012192;  
 GENBANK-AY012193; GENBANK-AY012194; GENBANK-AY012195;  
 GENBANK-AY012196; GENBANK-AY012197; GENBANK-AY012198;  
 GENBANK-AY012199; GENBANK-AY012200; GENBANK-AY012201  
 ENTRY MONTH: 200109  
 ENTRY DATE: Entered STN: 1 Oct 2001  
 Last Updated on STN: 1 Oct 2001  
 Entered Medline: 27 Sep 2001

## ABSTRACT:

The evolutionary history of the GDP-mannose pathway in *Salmonella enterica* was studied via sequencing *manB* and *manC* genes from 13 representative strains for O antigens containing mannose and/or sugar derivatives of GDP-D-mannose. In addition, colanic acid (CA) *manB* and *manC* genes were sequenced from selected strains, as the basis for a detailed comparison. Interestingly, including the eight previously characterized O antigen gene clusters, 12 of the 21 *S. enterica* strains studied in total (each representing a different O antigen structure) possess a *manB* gene which displays DNA identity, ranging from 93 to 99%, to the CA *manB* gene of *S. enterica* LT2. Furthermore, the CA-like *manB* genes (as well as the CA *manB* and *manC* genes) display subspecies specificity, and the CA and CA-like *manB* genes (for individual strains) appear to be evolving in concert via gene conversion events. In comparison, the *manC* genes were generally not CA-like, a situation also apparent in *Escherichia coli*, and therefore most strongly reflected the evolutionary history of the *S. enterica* O antigen GDP-mannose pathway. It appears that, in relatively recent times, gene capture from a distant source has occurred infrequently, and that groups of *manB* and *manC* genes have been maintained and are continuing to evolve within *S. enterica* and more closely related species.

CONTROLLED TERM: \*Bacterial Proteins: GE, genetics  
 Bacterial Proteins: ME, metabolism  
 Base Sequence  
 Cloning, Molecular  
 \*Evolution, Molecular  
 \*Guanosine Diphosphate Mannose: GE, genetics  
 Guanosine Diphosphate Mannose: ME, metabolism  
 \*Mannose-6-Phosphate Isomerase: GE, genetics  
 Mannose-6-Phosphate Isomerase: ME, metabolism  
 Molecular Sequence Data  
 \*Multienzyme Complexes: GE, genetics  
 Multienzyme Complexes: ME, metabolism  
 \*Nucleotidyltransferases: GE, genetics  
 Nucleotidyltransferases: ME, metabolism  
 O Antigens: GE, genetics  
 Phylogeny  
 Polysaccharides: GE, genetics  
 \*Salmonella enterica: GE, genetics

Sequence Analysis, DNA  
 CAS REGISTRY NO.: 3123-67-9 (Guanosine Diphosphate Mannose); 9012-87-7 (colanic acid)  
 CHEMICAL NAME: 0 (Bacterial Proteins); 0 (Multienzyme Complexes); 0 (O Antigens); 0 (Polysaccharides); EC 2.7.7.- (ManB protein, bacteria); EC 2.7.7.- (Nucleotidyltransferases); EC 5.3.1.8 (Mannose-6-Phosphate Isomerase)

L138 ANSWER 10 OF 25 MEDLINE on STN  
 ACCESSION NUMBER: 1981117027 MEDLINE Full-text  
 DOCUMENT NUMBER: PubMed ID: 7462153  
 TITLE: Reducing terminus of O-hapten accumulated in a Salmonella montevideo gale mutant.  
 AUTHOR: Heasley F A  
 CONTRACT NUMBER: AI-09644 (United States NIAID NIH HHS)  
 GM 07232 (United States NIGMS NIH HHS)  
 SOURCE: Journal of bacteriology, (1981 Jan) Vol. 145, No. 1, pp. 624-7.  
 Journal code: 2985120R. ISSN: 0021-9193. L-ISSN: 0021-9193.  
 Report No.: NLM-PMC217313.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 198104  
 ENTRY DATE: Entered STN: 16 Mar 1990  
 Last Updated on STN: 6 Feb 1998  
 Entered Medline: 24 Apr 1981

## ABSTRACT:

The O-haptenic polysaccharide of Salmonella montevideo has been reported to contain glyceraldehyde at its reducing terminus. However, O-hapten preparations from a *pmi* gale mutant contained products of partial hydrolysis of lipopolysaccharide, which in separate experiments gave [3H]glycerol upon treatment with perchloric acid and [3H]aBH<sub>4</sub>. Further study of the O-hapten reducing terminus suggested that it was actually mannose.

CONTROLLED TERM: Glycerol: AN, analysis  
 \*Haptens: AN, analysis  
 Hydrolysis  
 \*Lipopolysaccharides: AN, analysis  
 Mannose: AN, analysis  
 Mutation  
 Salmonella: GE, genetics  
 \*Salmonella: IM, immunology

CAS REGISTRY NO.: 31103-86-3 (Mannose); 56-81-5 (Glycerol)  
 CHEMICAL NAME: 0 (Haptens); 0 (Lipopolysaccharides)  
 MEDLINE REFERENCE COUNT: 10 There are 10 cited references available in MEDLINE for this document.

## REFERENCE(S): CITED REFERENCES AVAILABLE IN MEDLINE

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L138 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2007:483512 CAPLUS Full-text

DOCUMENT NUMBER: 147:89645

TITLE: Molecular characterization of the Fur protein of  
*Listeria monocytogenes*

AUTHOR(S): Ledala, Nagender; Pearson, Stacy L.; Wilkinson, Brian  
 J.; Jayaswal, R. K.

CORPORATE SOURCE: Microbiology Group, Department of Biological Sciences,  
 Illinois State University, Normal, IL, 61790-4120, USA

SOURCE: Microbiology (Reading, United Kingdom) (2007), 153(4),  
 1103-1111

CODEN: MROBEO; ISSN: 1350-0872

PUBLISHER: Society for General Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Iron is essential for the survival of almost all organisms, although excess iron can result in the generation of free radicals which are toxic to cells. To avoid the toxic effects of free radicals, the concentration of intracellular iron is generally regulated by the ferric uptake regulator Fur in bacteria. The 150 aa fur ORF from *Listeria monocytogenes* was cloned into pRSETa, and the His-tagged fusion protein was purified by nickel affinity column chromatog. DNA binding activity of this protein was studied by an electrophoretic mobility shift assay using the end-labeled promoters PphuDC and P<sub>fur</sub>. The results showed a decrease in migration for both promoter DNAs in the presence of the Fur protein, and the change in migration was competitively inhibited with an excess of the same unlabeled promoters. No shift in migration was observed when a similar assay was performed using non-specific end-labeled DNA. The assay showed that binding of Fur to P<sub>fur</sub> or PphuDC was independent of iron or manganese ions, and was not inhibited in the presence of 2 mM EDTA. Inductively coupled plasma MS of the Fur protein showed no iron or manganese, but 0.48 mol zinc per mol protein was detected. A DNase I protection assay revealed that Fur specifically bound to and protected a 19 bp consensus Fur box sequence located in the promoters of fur and phuDC. There was no requirement for iron or manganese in this assay also. However, Northern blot anal. showed an increase in fur transcription under iron-restricted compared to high-level conditions. Thus, the study suggests that under in vitro conditions, the affinity of the Fur protein for the 19 bp Fur box sequence does not require iron, but iron availability regulates fur transcription in vivo. Thus, the regulation by Fur in this intracellular pathogen may be dependent on either the structure of the DNA binding domain or other intracellular factors yet to be identified.

CC 6-3 (General Biochemistry)

Section cross-reference(s): 3, 10

IT Promoter (genetic element)

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (P<sub>fur</sub>; mol. characterization of Fur protein of *Listeria*  
*monocytogenes*)

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD  
 (3 CITINGS)

REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L138 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2002:900027 CAPLUS Full-text

DOCUMENT NUMBER: 138:132842  
 TITLE: Autoregulation of Helicobacter pylori Fur revealed by functional analysis of the iron-binding site  
 AUTHOR(S): Delany, Isabel; Spohn, Gunther; Pacheco, Ana-Beatriz F.; Ieva, Raffaele; Alaimo, Cristina; Rappuoli, Rino; Scarlato, Vincenzo  
 CORPORATE SOURCE: Department of Molecular Biology, IRIS, Chiron S.p.A., Siena, 53100, Italy  
 SOURCE: Molecular Microbiology (2002), 46(4), 1107-1122  
 CODEN: MOMIEE; ISSN: 0950-382X  
 PUBLISHER: Blackwell Science Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The ferric uptake regulator protein Fur regulates iron-dependent gene expression in bacteria. In Helicobacter pylori it has been shown to regulate iron-activated and iron-repressed genes. In this study, we show that H. pylori Fur protein regulates transcription from its own  $\sigma$ 80 promoter P<sub>fur</sub> in response to iron. Footprinting anal. shows that Fur binds at three distinct operators at P<sub>fur</sub> overlapping and proximal to the promoter elements. Site-directed mutagenesis of the proposed iron-binding site of the protein results in derepression of P<sub>fur</sub> and the loss of iron regulation. In vivo oligomerization assays reveals that the C-terminus of Fur is necessary for multimerization of the protein and that the mutations do not affect this activity. Mol. and phenotypic anal. of the mutant proteins provides evidence that the iron-binding site controls the specific affinity of Fur for the operators at P<sub>fur</sub> and hence its repressive ability. In summary, the data presented are consistent with a model in which Fur acts as a rheostat of transcription to autoregulate its own expression in response to iron, which in turn controls expression of iron-induced and iron-repressed genes, providing maintenance of homeostasis.

CC 6-3 (General Biochemistry)  
 Section cross-reference(s): 10

IT Transcription factors

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (Fur (ferric uptake regulation); Fur protein from Helicobacter pylori regulates transcription from P<sub>fur</sub> promoter in response to iron)

IT Molecular association

(Fur protein from Helicobacter pylori binds to multiple operators at P<sub>fur</sub> promoter overlapping and proximal to promoter elements)

IT Helicobacter pylori

Transcriptional regulation

(Fur protein from Helicobacter pylori regulates transcription from P<sub>fur</sub> promoter in response to iron)

IT Promoter (genetic element)

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (Fur protein from Helicobacter pylori regulates transcription from P<sub>fur</sub> promoter in response to iron)

IT Genetic element

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (operator; Fur protein from Helicobacter pylori binds to multiple operators at P<sub>fur</sub> promoter overlapping and proximal to promoter elements)

IT 7439-89-6, Iron, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (Fur protein from Helicobacter pylori regulates transcription from P<sub>fur</sub> promoter in response to iron)

OS.CITING REF COUNT: 35 THERE ARE 35 CAPLUS RECORDS THAT CITE THIS RECORD (35 CITINGS)

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L138 ANSWER 13 OF 25 WPIX COPYRIGHT 2010 THOMSON REUTERS on STN  
 DUPLICATE 2  
 ACCESSION NUMBER: 2008-E83936 [200833] WPIX  
 DOC. NO. CPI: C2008-160138 [200833]  
 TITLE: New live vaccine composition comprising a live attenuated  
 Salmonella bacterium, useful for protecting an animal  
 against avian influenza infection  
 DERWENT CLASS: B04; C06; D16  
 INVENTOR: BERMUDEZ D G; BERMUDEZ D  
 PATENT ASSIGNEE: (AVID-N) AVIDEX; (BERM-I) BERMUDEZ D G  
 COUNTRY COUNT: 121

## PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2008039408	A2	20080403	(200833)*	EN	55[11]	
US 20080124355	A1	20080529	(200838)	EN		
WO 2008039408	A3	20080710	(200847)	EN		
EP 2081593	A2	20090729	(200950)	EN		
IN 2009KN01483	A	20090529	(200951)	EN		
AU 2007300519	A1	20080403	(200953)	EN		
CN 101720228	A	20100602	(201040)	ZH		
CA 2700218	A1	20080403	(201045)	EN		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2008039408	A2	WO 2007-US20578	20070924
US 20080124355	A1 Provisional	US 2006-826542P	20060922
US 20080124355	A1	US 2007-859569	20070921
AU 2007300519	A1	AU 2007-300519	20070924
CN 101720228	A	CN 2007-80043473	20070924
EP 2081593	A2	EP 2007-838725	20070924
EP 2081593	A2 PCT Application	WO 2007-US20578	20070924
IN 2009KN01483	A PCT Application	WO 2007-US20578	20070924
CN 101720228	A PCT Application	WO 2007-US20578	20070924
IN 2009KN01483	A	IN 2009-KN1483	20090421
CA 2700218	A1	CA 2007-2700218	20070924
CA 2700218	A1 PCT Application	WO 2007-US20578	20070924
CA 2700218	A1 PCT Nat. Entry	CA 2007-2700218	20100319

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 2081593	A2 Based on	WO 2008039408 A
AU 2007300519	A1 Based on	WO 2008039408 A
CN 101720228	A Based on	WO 2008039408 A
CA 2700218	A1 Based on	WO 2008039408 A

PRIORITY APPLN. INFO: US 2007-859569 20070921  
 US 2006-826542P 20060922

INT. PATENT CLASSIF.:

MAIN: A61K039-112  
 IPC ORIGINAL: A61K0039-02 [I,A]; A61K0039-02 [I,C]; A61K0039-02 [I,A];  
 A61K0039-02 [I,C]; A61K0039-112 [I,A]; A61K0039-112 [I,C]  
 ; A61K0039-112 [I,C]; A61K0039-112 [I,A]; A61K0039-112  
 [I,C]; A61K0039-145 [I,A]; A61K0039-145 [I,C];  
 A61K0039-295 [I,A]; A61K0039-295 [I,C]; A61K0039-295  
 [I,A]; A61K0039-295 [I,C]; A61P0031-00 [I,C]; A61P0031-16  
 [I,A]; C12N0001-21 [I,A]; C12N0001-21 [I,C]  
 ECLA: A61K0039-145; C12N0001-36; C12N0009-24  
 ICO: K61K0039:52B; K61K0039:52C; K61K0039:54A1; K61K0039:55V;  
 M12N0760:05A  
 USCLASS NCLM: 424/200.100  
 NCLS: 435/252.300  
 BASIC ABSTRACT:

WO 2008039408 A2 UPAB: 20090806

NOVELTY - A new live vaccine composition for protecting an animal against avian influenza infection comprises a live attenuated *Salmonella* bacterium comprising: (1) an attenuating mutation in a genetic locus of the chromosome of the bacterium that attenuates virulence of the bacterium; or (2) an antigen-expressing DNA construct comprising a nucleotide sequence coding for an immunogenic polypeptide comprising an avian influenza H or N antigen and/or an immunogenic portion of the H or N antigen.

DETAILED DESCRIPTION - The new live vaccine composition for protecting an animal against avian influenza infection comprises a live attenuated *Salmonella* bacterium comprising: (1) an attenuating mutation in a genetic locus of the chromosome of the bacterium that attenuates virulence of the bacterium; or (2) an antigen-expressing DNA construct comprising a nucleotide sequence coding for an immunogenic polypeptide comprising an avian influenza H or N antigen and/or an immunogenic portion of the H or N antigen. The nucleotide sequence is operably linked to a promoter that permits expression of the immunogenic polypeptide from the DNA construct. The gene coding for the immunogenic polypeptide has at least one codon optimized for bacterial expression. The live vaccine composition elicits an immune response to at least one avian influenza antigen when administered orally to an animal.

INDEPENDENT CLAIMS are:

(1) a method of immunizing an animal against avian influenza; and (2) a kit adapted to be used to produce the live vaccine composition.

ACTIVITY - Virucide. No biological data given.

MECHANISM OF ACTION - Vaccine.

USE - The live vaccine composition comprising a live attenuated *Salmonella* bacterium is useful for protecting an animal against avian influenza infection (claimed).

TECHNOLOGY FOCUS:

BIOTECHNOLOGY - Preferred Composition: The live attenuated *Salmonella* bacterium is *Salmonella typhimurium*. The attenuating mutation is in a genetic locus comprising *phoP*, *phoQ*, *Mt*, *cya*, *crp*, *poxA*, *rpoS*, *htrA*, *nuoG*, *pmi*, *gale*, *pabA*, *pts*, *damA*, *purA*, *purB*, *purl*, *zwf*, *ompR* and/or *Suwwan*. The attenuating mutation is a deletion mutation. The attenuating mutation comprises at least a partial deletion mutation of *phoP*. The *Salmonella* bacterium comprises a lethal mutation, comprising a deletion in the *asd* gene. The immunogenic polypeptide comprises a fusion protein comprising a V antigen or its immunogenic portion linked to an F1 antigen, encoded on an antigen-expressing multi-copy plasmid. The origin of replication of the multi-copy plasmid is a *ColE1*, *pUC*, *M15* or *pBR322* plasmid origin of replication. The live attenuated *Salmonella* bacterium is genetically stabilized against genetic exchange with other organisms with respect to a wild type *Salmonella* of the same serovar. The live attenuated *Salmonella* bacterium is genetically stabilized with respect to a wild type *Salmonella* of the same serovar.



The live vaccine composition is produced from a kit comprising: (a) a first container comprising a bacterial expression codon optimized antigen from a pathogenic avian influenza virus strain containing unique genetically engineered restriction sites contained within at least one of a bacterial protein expression plasmid or a bacterial chromosomal protein expression vector which allows rapid exchange of small segments; and (b) a second container comprising bacterial flagellar vectors having at least one bacterial flagellar antigens. The Salmonella bacterium comprises multiple unique chromosomal localization vectors targeting at least IS200s, phage elements and metabolic genes for insertion of the expression codon. Preferred Kit: The kit further comprises a bacterial strain; where the bacterial expression codon allows rapid exchange of small segments, where the bacterial strain comprises multiple unique chromosomal localization vectors targeting at least IS200s, phage elements and metabolic genes for insertion of the expression codon. Preferred Method: Immunizing an animal against avian influenza comprises administering the live vaccine composition comprising a Salmonella bacterium that expresses an avian influenza H or N antigen, or an immunogenic portion of the H or N antigen. The live attenuated Salmonella bacterium is genetically stabilized through deletion of IS200 elements and bacteria phage and prophage elements, and genetically isolated from external phage infection by a constitutive expression of a P22 phage repressor.

## EXTENSION ABSTRACT:

EXAMPLE - No suitable example given.

FILE SEGMENT: CPI

MANUAL CODE: CPI: B04-F10A8; B04-F10A8E; B14-A02B2; B14-G01; B14-S11A; B14-S11D2; B14-S12; C04-F10A8; C04-F10A8E; C14-A02B2; C14-G01; C14-S11A; C14-S11D2; C14-S12; D05-H07

L138 ANSWER 14 OF 25 WPIX COPYRIGHT 2010 THOMSON REUTERS on STN  
 ACCESSION NUMBER: 2010-M57584 [201066] WPIX  
 TITLE: New salmonella enterica comprising protein glycosylation operon of Campylobacter jejuni derivative and presents N-glycan of Campylobacter jejuni derivative on its cell surface, useful for treating Salmonella infections  
 DERWENT CLASS: B04; C06; D13; D16  
 INVENTOR: AEBI M; AHUJA U; AMBER S; ILG K; SCHWARZ F  
 PATENT ASSIGNEE: (ETHE-C) EIDGENOESSISCHE TECH HOCHSCHULE ZUERICH  
 COUNTRY COUNT: 113

## PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2010108682	A1	20100930	(201066)*	EN	39	[4]

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2010108682	A1	WO 2010-EP1884	20100325

PRIORITY APPLN. INFO: EP 2009-4445 20090327

## INT. PATENT CLASSIF.:

IPC ORIGINAL: A61K0039-106 [I,A]; A61K0039-106 [I,C]; C07K0014-195 [I,C]; C07K0014-205 [I,A]; C12N0001-20 [I,A]; C12N0001-20 [I,C]; C12N0001-36 [I,A]; C12N0001-36 [I,C]

## BASIC ABSTRACT:

WO 2010108682 A1 UPAB: 20101014

NOVELTY - *Salmonella enterica* comprising at least one protein glycosylation (pgl) operon of *Campylobacter jejuni* or its functional derivative and presents at least one N-glycan of *Campylobacter jejuni* or its N-glycan derivative on its cell surface, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is/are included for production of the *Salmonella enterica*. ACTIVITY - Antibacterial; Antidiarrheic. Test details described, no results given.

MECHANISM OF ACTION - Vaccine.

USE - For preparing a medicament (preferably vaccine), pharmaceutical composition, food or feed, food or feed additive for the prevention and/or treatment of *Campylobacter jejuni* and *Salmonella* infections in human and animal including live stock such as cattle and poultry (all claimed).

ADVANTAGE - The *Salmonella* strain does not elicit pathogenic effects when administered to an animal or human in live and/or inactivated form.

#### TECHNOLOGY FOCUS:

BIOLOGY - Preparation (claimed): Production of *Salmonella enterica* involves: introducing into *Salmonella enterica* by at least one plasmid vector or by genomic integration at least one pgl operon of *Campylobacter jejuni* or its functional derivative (preferably at least one pgl operon, where at least one (preferably all) genes for bacillosamine biosynthesis are inactivated; and introducing mutations and/or deletions in the wbaP gene leading to complete inactivation of O-antigen biosynthesis. Preferred Species: The *Salmonella enterica* selected from *Salmonella typhimurium*, enteritidis, heidelberg, gallinarum, hadar, agona, kentucky and infantis, (preferably *Salmonella enterica* serovar typhimurium strains). The *Salmonella enterica* comprises at least one pgl operon, where at least one genes for bacillosamine biosynthesis are inactivated by mutation and/or partial or complete deletion, preferably by partial and/or complete deletion of the genes pgl D, E, F, G. The *Salmonella enterica* comprises at least one pgl operon, where the pglB gene product is inactivated by mutation and/or deletion. The *Salmonella enterica* (preferably serovar typhimurium strain) comprises: (a) at least one pgl operon of *Campylobacter jejuni* or its functional derivative (preferably at least one pgl operon, where at least one gene for bacillosamine biosynthesis are inactivated; and mutations and/or deletions in the wbaP gene leading to complete inactivation of O-antigen biosynthesis; and (b) and presents on its cell surface at least one of the N-glycan of *Campylobacter jejuni* or its N-glycan derivative. The N-glycans and their derivatives are linked to at least one homologous or heterologous *Salmonella* polypeptide that are transferred to and presented on the cell surface, preferably linked to at least one polypeptide comprising at least one consensus sequon Asn-Z'-Ser/Thr (preferably Asp/Glu-X-Asn-Z'-Ser/Thr (SEQ ID NO: 1). The N-glycans and their derivatives are linked to the *Salmonella* lipid A core or its functionally equivalent derivative. The *Salmonella* strain is attenuated, preferably by mutations selected from pab, pur, aro, aroA, asd, dap, nadA, pncB, gale, gmi, fur, rpsL, ompR, htrA, hemA, cdt, cya, crp, phoP, phoQ, rfc, poxA or galU, (preferably mutations aroA, cya or crp). The *Salmonella* strain is attenuated by partial or full inactivation of the expression of the O-antigen, (preferably by at least one mutation and/or deletion in the rfb gene cluster, especially in the wbaP gene, particularly deletion of the wbaP gene).

X and Z'=natural amino acid except Pro.

ORGANIC CHEMISTRY - Preferred Components: The N-glycan derivative is GalNAc- $\alpha$ 1,4-GalNAc- $\alpha$ 1,4-(Glc-  $\beta$ 1,3)GalNAc- $\alpha$ 1,4-GalNAc- $\alpha$ 1,4-GalNAc- $\alpha$ 1,3-2,4-diacetamido-2,4,6-trideoxy-D-glucopyranose (I); or GalNAc- $\alpha$ 1,4-GalNAc- $\alpha$ 1,4-(Glc-  $\beta$ 1,3)GalNAc- $\alpha$ 1,4-GalNAc- $\alpha$ 1,4-GalNAc- $\alpha$ 1,3-GlcNAc (II).

#### EXTENSION ABSTRACT:

ADMINISTRATION - Administration is intravenous, intramuscular, subcutaneous, intranasal, intrasynovial, by infusion, sublingual, transdermal, oral, topical or by inhalation. No dosage details given. EXAMPLE - No suitable example given.

FILE SEGMENT: CPI  
 MANUAL CODE: CPI: B04-F10A8E; B14-A01A8; B14-S11D2; C04-F10A8E;  
 C14-A01A8; C14-S11D2; D03-G01; D03-H01T2B; D05-H08;  
 D05-H14A1

L138 ANSWER 15 OF 25 WPIX COPYRIGHT 2010 THOMSON REUTERS on STN  
 ACCESSION NUMBER: 2000-302849 [200026] WPIX  
 DOC. NO. CPI: C2000-091734 [200026]  
 TITLE: New live attenuated Salmonella vaccines used for  
 protecting poultry against infection by avian pathogenic  
 gram-negative bacteria comprise an rfb/rfc gene cluster  
 of the bacteria stably integrated in Salmonella  
 chromosome  
 DERWENT CLASS: B04; C06; D16  
 INVENTOR: ROLAND K L  
 PATENT ASSIGNEE: (MEGA-N) MEGAN HEALTH INC  
 COUNTRY COUNT: 85

## PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2000004919	A2	20000203	(200026)*	EN	48[5]	
AU 9949914	A	20000214	(200029)	EN		
EP 1100536	A2	20010523	(200130)	EN		
ZA 2001000976	A	20011031	(200173)	EN	70	
CN 1315871	A	20011003	(200205)	ZH		
BR 9912410	A	20020115	(200214)	PT		
US 6399074	B1	20020604	(200242)	EN		
JP 2002521345	T	20020716	(200261)	JA	68	
MX 2001000884	A1	20020601	(200365)	ES		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000004919	A2	WO 1999-US15842	19990713
US 6399074	B1	US 1998-122441	19980724
AU 9949914	A	AU 1999-49914	19990713
BR 9912410	A	BR 1999-12410	19990713
CN 1315871	A	CN 1999-810045	19990713
EP 1100536	A2	EP 1999-933977	19990713
EP 1100536	A2	WO 1999-US15842	19990713
BR 9912410	A	WO 1999-US15842	19990713
JP 2002521345	T	WO 1999-US15842	19990713
MX 2001000884	A1	WO 1999-US15842	19990713
JP 2002521345	T	JP 2000-560912	19990713
MX 2001000884	A1	MX 2001-884	20010124
ZA 2001000976	A	ZA 2001-976	20010205

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9949914	A	WO 2000004919
EP 1100536	A2	WO 2000004919

BR 9912410 A	Based on	WO 2000004919 A
JP 2002521345 T	Based on	WO 2000004919 A
MX 2001000884 A1	Based on	WO 2000004919 A

PRIORITY APPLN. INFO: US 1998-122441 19980724

INT. PATENT CLASSIF.:

MAIN: A61K039-112

IPC RECLASSIF.: A61K0039-02 [I,A]; A61K0039-02 [I,C]; A61K0039-112 [I,A];  
A61K0039-112 [I,C]; A61K0039-116 [I,A]; A61K0039-116  
[I,C]; A61P0031-00 [I,C]; A61P0031-04 [I,A]; C07K0014-195  
[I,C]; C07K0014-245 [I,A]; C07K0014-255 [I,A]

ECLA: A61K0039-02T3; A61K0039-116; C07K0014-245; C07K0014-255

ICO: K61K0039:55V

JAP. PATENT CLASSIF.:

MAIN/SEC.: A61K0039-112; A61P0031-04 171

FTERM CLASSIF.: 4C085; 4C201; 4C206; 4C085/AA03; 4C085/BA24; 4C085/CC04;  
4C085/DD62; 4C085/EE01

BASIC ABSTRACT:

WO 2000004919 A2 UPAB: 20060116

NOVELTY - A vaccine (I) for immunization of birds against an avian pathogenic gram-negative (APGN) microbe (II), is new.

DETAILED DESCRIPTION - A vaccine (I) for immunization of birds against an avian pathogenic gram-negative (APGN) microbe (II), is new and comprises live cells of a recombinant Salmonella strain (III) expressing an O-antigen of (II), and having:

(1) a rfb/rfc gene cluster of (II) stably integrated into the Salmonella chromosome; and  
(2) a mutation in the rfb gene cluster or rfc gene of (III) which inactivates expression of the O-antigen, where (III) is an attenuated mutant of a virulent Salmonella strain.

INDEPENDENT CLAIMS are also included for the following: (1) a method (IV) for immunizing a bird against an APGN microbe, comprising administering (I) to the bird; (2) a vaccine (V) for immunization of birds against at least two APGN microbes, comprising a mixture of live cells of first and second recombinant Salmonella strains, each strain having the features of (1) and (2) above; (3) a vaccine (VI) for immunization of birds against at least two APGN microbes, comprising live cells of a recombinant Salmonella strain expressing an O-antigen of each of the APGN microbes, and having a rfb/rfc gene cluster of each of the APGN microbes stably integrated into the Salmonella chromosome, and having a mutation in the Salmonella rfb gene cluster or rfc gene which inactivates expression of the Salmonella O-antigen, wherein the recombinant Salmonella strain is an attenuated mutant of a virulent Salmonella strain; and (4) a method (VII) of making a vaccine for immunizing a bird against an APGN microbe.

USE - The vaccines are used to immunize birds against pathogenic gram negative bacteria, especially avian pathogenic Escherichia coli (APEC), which cause diseases such as air sacculitis, cellulitis, colibacillosis, and peritonitis. Birds which may be immunized include geese, pheasants, and other domesticated birds, especially chickens and turkeys as well as non-domesticated birds such as parrots and parakeets. The recombinant Salmonella strain can also be used to deliver a desired gene product to the vaccinated bird. The avirulent microbes can be used as vectors for the synthesis of other proteins, including immunoregulatory molecules made by avian species that might stimulate or suppress various physiological functions such as growth rate, fat or protein content.

ADVANTAGE - As (I) is an oral vaccine, it costs less to produce and is easier to administer in the field than an injectable vaccine. The recombinant Salmonella strain protects against both the gram negative microbe and the parental Salmonella strain. Also, as Salmonella sp. persist in the gut, they provide a more vigorous immune response. TECHNOLOGY FOCUS:

**BIOLOGY - Preferred Microbe:** The APGN microbes include avian pathogenic *Salmonella* strains of group C and D, species of *Campylobacter*, *Bacteroides*, *Bordetella*, *Haemophilus*, *Pasteurella*, *Francisella*, *Actinobacillus*, *Klebsiella*, *Moraxella*, *Pseudomonas*, *Proteus*, and *Ornithobacterium* and preferably, avian pathogenic *Escherichia coli* (APEC) strains 03, 06, 08, 015, 071, 074, 087, 088, 095, 0103 and 0109.

**BIOTECHNOLOGY - Preparation:** (VII) comprises selecting a *Salmonella* strain capable of colonizing the bird, integrating into the *Salmonella* chromosome an *rfb/rfc* gene cluster from the APGN microbe, introducing a mutation into the *Salmonella rfb* gene cluster and/or into the *rfc* gene and isolating recombinant *Salmonella* bacteria which expresses O-antigen characteristic of the APEC (avian pathogenic *Escherichia coli*) strain but which do not express *Salmonella* O-antigen. The integration and introducing steps can be performed in any order. The selected *Salmonella* strain is preferably a virulent strain, and the method also comprises introducing into the virulent *Salmonella* strain an attenuating mutation in a gene selected from *pab*, *pur*, *aro*, *asd*, *dap*, *nadA*, *pncB*, *galE*, *pmi*, *fur*, *rpsL*, *ompR*, *htrA*, *hemA*, *cdt*, *cya*, *crp*, *phoP*, *phoQ*, *rfc*, *poxA*, *galU*, and then isolating mutant having attenuated virulence.

**Preferred Vaccine:** The integrated *rfb/rfc* gene cluster comprises an attenuating mutation in a *Salmonella* gene selected from *pab*, *pur*, *aro*, *asd*, *dap*, *nadA*, *pncB*, *galE*, *pmi*, *fur*, *rpsL*, *ompR*, *htrA*, *hemA*, *cdt*, *cya*, *crp*, *phoP*, *phoQ*, *rfc*, *poxA*, *galU*. The attenuating mutation is especially a defined deletion/insertion in the *Salmonella crp* gene, and the recombinant *Salmonella* also has an attenuating mutation in the *crp* gene. The recombinant *Salmonella* strain also has a recombinant polynucleotide encoding a desired gene product, which is especially an antigen from an avian pathogenic organism, such as a APEC fimbriae or an iron-regulated outer membrane protein.

#### EXTENSION ABSTRACT:

**ADMINISTRATION -** (I) is administered by coarse spray at the day of hatching, followed by oral administration of a booster amount of the vaccine, especially at day 13, 14 or 15 after the day of hatching. Dosage is in concentrations ranging from 10<sup>5</sup> to 10<sup>8</sup> live cells per bird, preferably 5x10<sup>7</sup> live cells/bird. **SPECIFIC MICROORGANISMS -** The APGN microbe is especially avian pathogenic *Escherichia coli* (APEC) strain 01, 02, 035 or 078. **EXAMPLE -** A recombinant *Salmonella typhimurium* strain coexpressing *S. typhimurium* group B lipopolysaccharide (LPS) and *Escherichia coli* 078 LPS was created and designated MGN996. The chickens used were White leghorns hatched from fertile eggs from specific pathogen-free chickens. The birds were vaccinated twice, once at day of hatch and again at 14 days of age. Chickens were inoculated at day of hatch with 4.6 x 10<sup>6</sup> CFU of MGN996 per chick by coarse spray. 26 birds were vaccinated with MGN996 and 12 chick were mock vaccinated with BSG (undefined). At day 14, vaccinated birds were boosted with 3.8 x 10<sup>7</sup> CFU of MGN996 orally. On day 28, all birds were challenged with 7.5 x 10<sup>7</sup> CFU of *E. coli* strain x 7122 intratracheally. Four days later, the birds were euthanized by CO<sub>2</sub> inhalation, and necropsied. The birds were scored for lesions associated with avian pathogenic *E. coli* (APEC) infection. The mean lesions indicated that birds vaccinated with MGN996 were significantly protected from challenge when compared to non-vaccinated control birds. In addition, vaccinated birds showed a significant reduction in overall mean lesion scores.

#### FILE SEGMENT:

CPI

#### MANUAL CODE:

CPI: B04-B04C1; B04-E02F; B04-F10A8E; B11-C08E5;  
B12-K04F; B14-A01A3; B14-S03; C04-B04C1; C04-E02F;  
C04-F10A8E; C11-C08E5; C12-K04F; C14-A01A3; C14-S03;  
D05-H07; D05-H12A; D05-H14A1; D05-H18

L138 ANSWER 16 OF 25 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on  
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ACCESSION NUMBER: 1982:266644 BIOSIS Full-text

DOCUMENT NUMBER: PREV198274039124; BA74:39124

TITLE: MUTATIONS IN SALMONELLA-  
TYPHIMURIUM AFFECTING SYNTHESIS OF LIPO POLY  
SACCHARIDE CORE AT HIGH TEMPERATURE.

AUTHOR(S): LERMAN R D [Reprint author]; STOCKER B A D

CORPORATE SOURCE: DEP MED MICROBIOL, STANFORD UNIV SCH MED, STANFORD, CA  
94305, USA

SOURCE: Wasmann Journal of Biology, (1981) Vol. 39, No. 1-2, pp.  
42-49.

CODEN: WMJBA2. ISSN: 0043-0927.

DOCUMENT TYPE: Article

FILE SEGMENT: BA

LANGUAGE: ENGLISH

ABSTRACT: S. typhimurium mutants of class rfaH cannot form the  
galactose I unit of the lipopolysaccharide (LPS) core and so are resistant to  
phage FO but sensitive to phage C21. To test whether gene rfaH specifies the  
galactose transferase or a protein regulating its synthesis, rfaH  
\*\*\*mutants\*\*\* making galactose-deficient LPS when grown at 43° C but  
normal LPS at 30° C (using as parents pmi mutants,  
unable to make O side-chains of LPS unless supplied with mannose) were used.  
Of 120 mutagen-induced FO-resistant mutants isolated at 43°  
C, 20 were FO-sensitive at 30° C and 6 were sensitive to C21 at  
43° C. The C21 resistant mutants may be  
temperature-sensitive rfaH mutants.

CONCEPT CODE: Biochemistry studies - Proteins, peptides and amino acids  
10064

Biochemistry studies - Lipids 10066

External effects - Temperature as a primary variable  
10614

Enzymes - Physiological studies 10808

Metabolism - Carbohydrates 13004

Metabolism - Lipids 13006

Metabolism - Proteins, peptides and amino acids 13012

Temperature - General measurement and methods 23001

Physiology and biochemistry of bacteria 31000

Genetics of bacteria and viruses 31500

Virology - Bacteriophage 33504

INDEX TERMS: Major Concepts

Enzymology (Biochemistry and Molecular Biophysics);  
Genetics; Metabolism; Microbiology; Physiology

INDEX TERMS: Miscellaneous Descriptors

PHAGE FO PHAGE C-21 GALACTOSE TRANSFERASE REGULATORY  
PROTEIN TEMPERATURE SENSITIVE MUTANTS RFA-H  
GENE

ORGANISM: Classifier

Viruses 03000

Super Taxa

Microorganisms

Taxa Notes

Microorganisms, Viruses

ORGANISM: Classifier

Enterobacteriaceae 06702

Super Taxa

Facultatively Anaerobic Gram-Negative Rods; Eubacteria;  
Bacteria; Microorganisms

Taxa Notes  
Bacteria, Eubacteria, Microorganisms

L138 ANSWER 17 OF 25 DISSABS COPYRIGHT (C) 2010 ProQuest Information and Learning Company; All Rights Reserved on STN

ACCESSION NUMBER: 90:23256 DISSABS Order Number: AAR9106359  
TITLE: THE TOPOLOGY OF THE TERMINAL STEPS OF O-ANTIGEN ASSEMBLY ON THE INNER MEMBRANE OF SALMONELLA TYPHIMURIUM  
AUTHOR: MCGRATH, BARBARA CLAIRE [PH.D.]; OSBORN, MARY JANE [advisor]  
CORPORATE SOURCE: THE UNIVERSITY OF CONNECTICUT (0056)  
SOURCE: Dissertation Abstracts International, (1990) Vol. 51, No. 9B, p. 4194. Order No.: AAR9106359. 145 pages.  
DOCUMENT TYPE: Dissertation  
FILE SEGMENT: DAI  
LANGUAGE: English  
ENTRY DATE: Entered STN: 19921118  
Last Updated on STN: 19921118

ABSTRACT: Previous immunoelectron microscopic evidence (Mulford, C. A., Osborn, M. J. (1983) Proc. Natl. Acad. Sci. USA. 80:1159-1163) has demonstrated that O-reactive LPS is transiently localized to the periplasmic face of the inner membrane prior to its translocation to the outer membrane. Furthermore, undecaprenol-P-linked polymeric O antigen accumulates at the periplasmic face in mutants which are blocked in LPS core biosynthesis. The in vivo pulse-chase experiments described here provide evidence that ligation of O antigen to core occurs at the periplasmic face of the inner membrane. Mutants doubly conditional for core (*ΔkdsAts*) and O antigen (*ΔgalE*, *Δpmi*) when pulsed with ( $^3\text{H}$ ) mannose at nonpermissive temperature for core biosynthesis ( $42^\circ\text{C}$ ), accumulate radioactively labeled, undecaprenol-linked O antigen. Upon shift to permissive temperature ( $30^\circ\text{C}$ ), the radioactivity rapidly chases into LPS. Similar experiments on a mutant which is also defective in polymerization of O antigen (*rfc*-), show that accumulated undecaprenol-P-linked O antigen tetracosaccharide can also chase into LPS. This suggests that polymerization of O antigen also occurs at the periplasmic face of the inner membrane. Other pulse-chase experiments demonstrate that the in vivo transfer of previously accumulated polymeric O antigen to LPS core is blocked by the uncoupler 2,4 dinitrophenol (DNP). The results indicate that LPS core is synthesized in the presence of DNP, and is functional in an in vitro ligase assay. We therefore propose that the disruption of the membrane potential by DNP traps newly synthesized LPS core on the cytosolic face of the inner membrane, where it is inaccessible for ligation to the periplasmically oriented undecaprenol-linked O antigen.

CLASSIFICATION: 0307 BIOLOGY, MOLECULAR

L138 ANSWER 18 OF 25 LIFESCI COPYRIGHT 2010 CSA on STN

ACCESSION NUMBER: 81:59624 LIFESCI Full-text  
TITLE: Mutations in Salmonella typhimurium Affecting Synthesis of LPS Core at High Temperature.  
AUTHOR: Lerman, R.D.; Stocker, B.A.D.

CORPORATE SOURCE: Dep. Med. Microbiol., Stanford Univ. Sch. Med., Stanford, CA 94305, USA

SOURCE: WASMANN J. BIOL., (1981) vol. 39, no. 1-2.

DOCUMENT TYPE: Journal

FILE SEGMENT: G; J

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT: *Salmonella typhimurium* mutants of class rfaH cannot form the galactose I unit of the lipopolysaccharide (LPS) core and so are resistant to phage FO but sensitive to phage C21. To test whether gene rfaH specifies the galactose-transferase or a protein regulating its synthesis the authors sought rfaH mutants making galactose-deficient LPS when grown at 43 degree C but normal LPS at 30 degree C (using as parents pm1 mutants, unable to make O side-chains of LPS unless supplied with mannose). Of 120 mutagen-induced FO-resistant mutants isolated at 43 degree C 20 were FO-sensitive at 30 degree C; 6 were sensitive to C21 at 43 degree C and may be temperature-sensitive rfaH mutants.

CLASSIFICATION: 07320 Bacterial genetics; 02740 Genetics and evolution

UNCONTROLLED TERM: *Salmonella typhimurium*;  
temperature-sensitive mutant;  
lipopolysaccharides; genes; biosynthesis; effects on; rfaH gene; role

L138 ANSWER 19 OF 25 Elsevier Biobase COPYRIGHT 2010 Elsevier Science B.V. on STN

ACCESSION NUMBER: 2000000178 ESBIODASE Full-text

TITLE: The *Legionella pneumophila* prp locus required during infection of macrophages and amoebae

AUTHOR(S): Stone, Barbara J.; Brier, Adam; Kwaik, Yousef Abu

CORPORATE SOURCE: Stone, Barbara J.; Brier, Adam; Kwaik, Yousef Abu (Dept. of Microbiology and Immunology, Univ. of Kentucky Chandler Med. Ctr., Lexington, KY 40536-0084 (US))

SOURCE: Microbial Pathogenesis (Dec 1999) Volume 27, Number 6, pp. 369-376, 49 refs.  
CODEN: MIPAEV ISSN: 0882-4010  
DOI: 10.1006/mpat.1999.0311

COUNTRY OF PUBLICATION: United Kingdom

DOCUMENT TYPE: Journal; Article

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 31 Jan 2009  
Last updated on STN: 31 Jan 2009

ABSTRACT: Transposon mutagenesis was performed using mTn10phoA to identify *Legionella pneumophila* genes that are expressed under certain in vitro conditions, and are required for intracellular replication. Of the 1653 PhoA fusions examined, 19 PhoA + fusion mutants were isolated and screened for differential expression of fusion proteins after growth at 30 or 37°C, in the presence of low iron, or increased magnesium concentrations. The mutants were examined for their cytopathogenicity and intracellular replication within U937 macrophage-like cells and the protozoan *Hartmannella vermiformis*. One of the mutants generated, BS10, was defective in its multiplication within U937 macrophage-like cells and *H. vermiformis*. The defect in BS10 was complemented with a cosmid clone containing the wild type locus. The open reading frame interrupted by the insertion was homologous to prpD of *Salmonella typhimurium* and mmgE of *Bacillus subtilis*. CLASSIFICATION CODE: 84.3.7 GENETICS AND MOLECULAR BIOLOGY, PROKARYOTIC  
GENETICS, Genetics of Animal Pathogenesis; 85.7.13  
APPLIED MICROBIOLOGY AND BIOTECHNOLOGY, MICROBIAL



METABOLISM AND PHYSIOLOGY, Virulence Factors; 86.7.3.5  
 IMMUNOLOGY AND INFECTIOUS DISEASES, IMMUNITY TO  
 INFECTION, Medical and Veterinary Bacteriology,  
 Virulence

SUPPLEMENTARY TERM: Intracellular; Iron; PhoA; pmi; prpD  
 ORGANISM NAME: Animalia; Bacillus subtilis; Bacteria (microorganisms);  
 Hartmannella vermiformis; Legionella pneumophila;  
 Negibacteria; Protozoa; Salmonella typhimurium  
 ; Sarcodina; Typhimurium  
 GENE NUMBER: GENBANK AF157018 referred number

L138 ANSWER 20 OF 25 BIOTECHDS COPYRIGHT 2010 THOMSON REUTERS on STN

ACCESSION NUMBER: 1998-02067 BIOTECHDS Full-text

TITLE: Development of genetically defined avirulent salmonella  
 vaccines;  
 using Salmonella typhimurium deletion  
 mutants (conference abstract)

AUTHOR: Sundaram P; Tinge S; Kaniga K; Curtiss III R

CORPORATE SOURCE: MEGAN-Health

LOCATION: MEGAN Health Inc., 3655 Vista, St.Louis, MO, USA.

SOURCE: Abstr.Gen.Meet.Am.Soc.Microbiol.; (1997) 97 Meet., 288

CODEN: 0005P

ISSN: 0067-2777

American Society for Microbiology, 97th General Meeting,  
 Miami Beach, FL, 4-8 May, 1997.

DOCUMENT TYPE: Journal

LANGUAGE: English

ABSTRACT: Well-characterized, safe yet effective Salmonella vaccine  
 strains were successfully and rapidly constructed. Defined  
 deletions in the Salmonella typhimurium asd, cya, crp, phoP,  
 phoQ, phoPQ and pmi genes were generated and cloned into a pir  
 dependant replicon. These defined deletions were introduced  
 into the chromosome of a wild-type S. typhimurium strain and  
 either fusaric acid or sucrose counter selection was employed  
 to recover mutants containing the replaced alleles. Strains  
 with double mutations were constructed using combinations of  
 the single mutations and characterized for the expected mutant  
 phenotype. The cya crp, pmi crp, phoP, phoQ, phoPQ and phoP pmi  
 mutants were safe and immunogenic in BALB/c mice. (0 ref)

CLASSIFICATION: D PHARMACEUTICALS; D4 Vaccines; A GENETIC ENGINEERING AND  
 FERMENTATION; A1 Nucleic Acid Technology

CONTROLLED TERMS: SALMONELLA TYPHIMURIUM RECOMBINANT  
 VACCINE STRAIN PREP., CHARACTERIZATION BACTERIUM (VOL.17,  
 NO.5)

L138 ANSWER 21 OF 25 SCISEARCH COPYRIGHT (c) 2010 The Thomson Corporation on  
 STN

ACCESSION NUMBER: 1999:82016 SCISEARCH Full-text

THE GENUINE ARTICLE: 159PC

TITLE: Different fates of Legionella pneumophila pmi  
 and mil mutants within macrophages and alveolar  
 epithelial cells

AUTHOR: Abu Kwaik Y (Reprint)

CORPORATE SOURCE: Univ Kentucky, Albert B Chandler Med Ctr, Dept Microbiol &  
 Immunol, Lexington, KY 40536 USA (Reprint)

AUTHOR: Gao L Y; Stone B J; Brieland J K

CORPORATE SOURCE: Univ Michigan, Unit Lab Anim Med, Ann Arbor, MI 48109 USA

COUNTRY OF AUTHOR: USA

SOURCE: MICROBIAL PATHOGENESIS, (DEC 1998) Vol. 25, No. 6, pp.  
 291-306.

ISSN: 0882-4010.

PUBLISHER: ACADEMIC PRESS LTD, 24-28 OVAL RD, LONDON NW1 7DX, ENGLAND

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 50

ENTRY DATE: Entered STN: 1999

Last Updated on STN: 1999

## ABSTRACT:

Alveolar epithelial cells, which constitute the majority of the alveolar surface, may represent a potential niche for intracellular replication of *Legionella pneumophila* that has been largely overlooked. We examined the phenotypes of a bank of 121 macrophage-defective mutants of *L. pneumophila* (designated as *pml* and *mil*) for their cytopathogenicity to and intracellular survival and replication within human alveolar epithelial cells. Our data showed that 91 of 121 mutants that were defective (modest-severe) in macrophages exhibited wild type-like phenotypes in human type I alveolar epithelial cells. In contrast, the other 30 mutants were defective in both macrophages and alveolar epithelial cells. Transmission electron microscopy of the intracellular infection by three \*\*\*mutants\*\*\* showed that the defect in intracellular replication in macrophages and epithelial cells was associated with a defect in recruitment of the RER around the phagosome. Differences in attachment to macrophages and epithelial cells were also exhibited by some of the mutants. Pulmonary infection studies of A/J mice showed that a mutant defective in macrophages but not in alveolar epithelial cells replicated like the wild type strain in the lungs of A/J mice. In contrast, a mutant defective in both macrophages and alveolar epithelial cells failed to replicate and was killed. We conclude that certain distinct genetic loci of *L. pneumophila* are uniquely required for intracellular survival and replication within phagocytic but not epithelial cells, which may be important in vivo. (C) 1998 Academic Press.

CATEGORY: IMMUNOLOGY; MICROBIOLOGY

SUPPLEMENTARY TERM: intracellular; bacteria; macrophage; epithelial; pathogenesis; Legionnaires

SUPPL. TERM PLUS: LEGIONNAIRES-DISEASE BACTERIUM; SALMONELLA-TYPHIMURIUM; INTRACELLULAR INFECTION; PERITONEAL-MACROPHAGES; HUMAN-MONOCYTES; PHOP-PHOQ; A/J MICE; VIRULENCE; GROWTH; INVASION

## REFERENCE(S):

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG  (RPG)	Referenced Work (RWK)
ABUKWAIK Y	1998	66	203	INFECT IMMUN
ABUKWAIK Y	1993	61	1320	INFECT IMMUN
ABUKWAIK Y	1994	13	243	MOL MICROBIOL
ABUKWAIK Y	1996	21	543	MOL MICROBIOL
ABUKWAIK Y	1997	24	629	MOL MICROBIOL
ALPUCHEARANDA C M	1992	89	10079	P NATL ACAD SCI USA
ARATA S	1993	61	5056	INFECT IMMUN
BEHLAU I	1993	175	4475	J BACTERIOL
BERGER K H	1993	7	7	MOL MICROBIOL
BLANCHARD D K	1988	56	1187	INFECT IMMUN
BREIMAN R F	1990	161	1257	J INFECT DIS
BRIELAND J	1994	145	1537	AM J PATHOL
CARPO J D	1982	125	740	AM REV RESPIR DIS
CIANCIOOTTO N P	1990	162	121	J INFECT DIS
CIANCIOOTTO N P	1989	57	1255	INFECT IMMUN
CIANCIOOTTO N P	1992	89	5188	P NATL ACAD SCI USA
CIANCIOOTTO N P	1995	30	247	CURR MICROBIOL

FIELDS B S	1996	4	286	TRENDS MICROBIOL
FUJIO H	1992	89	183	FEMS MICROBIOL IMMUN
GAO L Y	1998	66	883	INFECT IMMUN
GAO L Y	1997	65	4738	INFECT IMMUN
GARCIADPORTILLO F	1995	129	81	J CELL BIOL
RODGERS F G	1993	39	718	CAN J MICROBIOL
HARB O S	1998	64	126	APPL ENVIRON MICROB
HORWITZ M A	1983	158	1319	J EXP MED
HORWITZ M A	1983	158	2108	J EXP MED
HUSMANN L K	1992	60	5212	INFECT IMMUN
KWAIK Y A	1996	62	2022	APPL ENVIRON MICROB
KWAIK Y A	1994	62	1860	INFECT IMMUN
MARRA A	1992	89	9607	P NATL ACAD SCI USA
MILLER S I	1989	86	5054	P NATL ACAD SCI USA
MILLER S I	1990	172	2485	J BACTERIOL
MILLER V L	1992	60	3763	INFECT IMMUN
MILLER S I	1991	5	2073	MOL MICROBIOL
MODY C H	1993	167	1138	J INFECT DIS
NASH T W	1984	74	771	J CLIN INVEST
OH Y K	1996	64	3877	INFECT IMMUN
PAYNE N R	1987	166	1377	J EXP MED
ROY C R	1998	28	663	MOL MICROBIOL
SAMBROOK J	1989			MOL CLONING LAB MANU
SEGAL G	1998	95	1669	P NATL ACAD SCI USA
STONE B J	1998	66	1768	INFECT IMMUN
SUSA M	1996	64	1679	INFECT IMMUN
SUSA M	1998	160	316	J IMMUNOL
VENKATARAMAN C	1997	186	537	J EXP MED
VESCOVI E G	1996	84	165	CELL
VOGEL J P	1998	279	873	SCIENCE
WINN W C	1981	12	401	HUM PATHOL
WINTERMEYER E	1995	63	4576	INFECT IMMUN
YAMAMOTO Y	1988	56	370	INFECT IMMUN

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ACCESSION NUMBER: 1999298518 EMBASE Full-text

TITLE: Attenuation and immunogenicity of  $\Delta$ cya  
 $\Delta$ crp derivatives of Salmonella choleraesuis in pigs.

AUTHOR: Kennedy, Michael J. (correspondence); Yancey Jr., Robert J.; Sanchez, Margaret S.; Rzepkowski, Robert A.

CORPORATE SOURCE: Animal Health Discovery Research, Vet. Infectious Diseases Section, Pharmacia and Upjohn, Inc., Kalamazoo, MI 49001, United States. Michael.J.Kennedy@am.pnu.com

AUTHOR: Kelly, Sandra M.

CORPORATE SOURCE: MEGAN Health, St. Louis, MO 63110, United States.

AUTHOR: Curtiss III, Roy

CORPORATE SOURCE: Washington University, St. Louis, MO 63130, United States.

AUTHOR: Kennedy, Michael J. (correspondence)

CORPORATE SOURCE: Animal Health Discovery Research, Vet. Infectious Diseases Section, Pharmacia and Upjohn, Inc., 7000 Portage Rd., Kalamazoo, MI 49001, United States. Michael.J.Kennedy@am.pnu.com

AUTHOR: Yancey Jr., Robert J.

CORPORATE SOURCE: Central Research Division, Pfizer Inc., Groton, CT 06340, United States.

AUTHOR: Kennedy, Michael J. (correspondence)

CORPORATE SOURCE: Animal Health Discovery Research, Veterinary Infect. Diseases Section, Pharmacia and Upjohn, Inc., 7000 Portage Rd., Kalamazoo, MI 49001, United States. Michael.J.Kennedy@

SOURCE: am.pnu.com  
 Infection and Immunity, (1999) Vol. 67, No. 9, pp.  
 4628-4636.  
 Refs: 47  
 ISSN: 0019-9567 CODEN: INFIBR  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 026 Immunology, Serology and Transplantation  
 004 Microbiology: Bacteriology, Mycology, Parasitology  
 and Virology  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 10 Sep 1999  
 Last Updated on STN: 10 Sep 1999

ABSTRACT: Six different isogenic  $\Delta$ cya  $\Delta$ crp derivatives of a strain of *Salmonella choleraesuis* var. kuzendorf- $\chi$ 3246 virulent for pigs were constructed by transposon-mediated deletion mutagenesis. These strains were evaluated for virulence and ability to elicit a protective immune response in young weaned pigs after oral administration and were compared to a commercially available vaccine which lacks the 50-kb virulence plasmid (vpl-). These derivatives were  $\Delta$ cya  $\Delta$ crp vpl+,  $\Delta$ cya  $\Delta$ crp vpl-,  $\Delta$ cya  $\Delta$ (crp-cdt) vpl+,  $\Delta$ cya  $\Delta$ (crp-cdt) vpl-,  $\Delta$ cya  $\Delta$ crp pmi3834 vpl+, and  $\Delta$ cya  $\Delta$ (crp-cdt) pmi-3834. In experiments to evaluate safety, no significant adverse effects of any of the vaccine constructs were observed, except that two of the strains which carried the virulence plasmid (vpl+) caused a small, short-term elevation in maximum temperature compared to pretreatment temperature values. Orally immunized animals, except for those vaccinated with the  $\Delta$ cya  $\Delta$ crp pmi-3834 vpl+ strain or SC-54, developed significant serum antibody responses 21 days postvaccination as measured by enzyme-linked immunosorbent assay. No cell-mediated immune responses to heat-killed *S. choleraesuis* were noted at the same time point as measured with heat-killed bacteria as antigen in a lymphocyte proliferation assay. In an oral challenge exposure model with a highly virulent heterologous strain of *S. choleraesuis*, the  $\Delta$ cya  $\Delta$ crp strains with deletions in pmi were not protective. As measured by morbidity scores, the responses to challenge of the pigs vaccinated with the other four  $\Delta$ cya  $\Delta$ crp derivatives were significantly better than those of the nonvaccinated, challenged group. With the exception of temperature elevation and slight differences in diarrhea scores postchallenge, none of these strains differed significantly from each other in the other clinical parameters analyzed. While the commercial vaccine was protective by most of the parameters measured, it was not fully protective against challenge with virulent *S. choleraesuis* as judged by diarrhea scores and temperature elevation. Collectively, these data demonstrate that  $\Delta$ cya  $\Delta$ crp derivatives, with or without the virulence plasmid but not with deletions in the pmi gene, are candidates for vaccines for protection against salmonellosis in pigs.

CONTROLLED TERM: Medical Descriptors:  
 animal cell  
 animal experiment  
 animal model  
 antibody response  
 article  
 \*bacterial virulence  
 cellular immunity  
 immunogenicity  
 lymphocyte proliferation

nonhuman  
 priority journal  
 \*salmonella choleraesuis  
 \*salmonellosis  
 scoring system  
 swine  
 CONTROLLED TERM: Drug Descriptors:  
 \*bacterial vaccine

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ACCESSION NUMBER: 1998319908 EMBASE Full-text  
 TITLE: Synthesis of the A-band polysaccharide sugar D-rhamnose requires Rmd and WbpW: Identification of multiple AlgA homologues, WbpW and ORF488, in *Pseudomonas aeruginosa*.  
 AUTHOR: Rocchetta, Heather L.; Pacan, Jennifer C.; Lam, Joseph S. (correspondence)  
 CORPORATE SOURCE: Department of Microbiology, Canadian Bacterial Diseases Network, University of Guelph, Guelph, Ont. N1G 2W1, Canada . jlam@uoguelph.ca  
 SOURCE: Molecular Microbiology, (1998) Vol. 29, No. 6, pp. 1419-1434.  
 Refs: 60  
 ISSN: 0950-382X CODEN: MOMIEE  
 COUNTRY: United Kingdom  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 004 Microbiology: Bacteriology, Mycology, Parasitology and Virology  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 15 Oct 1998  
 Last Updated on STN: 15 Oct 1998

ABSTRACT: *Pseudomonas aeruginosa* is capable of producing various cell-surface polysaccharides including alginate, A-band and B-band lipopolysaccharides (LPS). The D-mannuronic acid residues of alginate and the D-rhamnose (D-Rha) residues of A-band polysaccharide are both derived from the common sugar nucleotide precursor GDP-D-mannose (D-Man). Three genes, *rmd*, *gmd* and *wbpW*, which encode proteins involved in the synthesis of GDP-D-Rha, have been localized to the 5' end of the A-band gene cluster. In this study, *WbpW* was found to be homologous to phosphomannose isomerases (PMIs) and GDP-mannose pyrophosphorylases (GMPs) involved in GDP-D-Man biosynthesis. To confirm the enzymatic activity of *WbpW*, *Escherichia coli* PMI and GMP mutants deficient in the K30 capsule were complemented with *wbpW*, and restoration of K30 capsule production was observed. This indicates that *WbpW*, like *AlgA*, is a bifunctional enzyme that possesses both PMI and GMP activities for the synthesis of GDP-D-Man. No gene encoding a phosphomannose mutase (PMM) enzyme could be identified within the A-band gene cluster. This suggests that the PMM activity of *AlgC* may be essential for synthesis of the precursor pool of GDP-D-Man, which is converted to GDP-D-Rha for A-band synthesis. *Gmd*, a previously reported A-band enzyme, and *Rmd* are predicted to perform the two-step conversion of GDP-D-Man to GDP-D-Rha. Chromosomal mutants were generated in both *rmd* and *wbpW*. The *Rmd* mutants do not produce A-band LPS, while the *WbpW* mutants synthesize very low amounts of A band after 18 h of growth. The latter observation was thought to result from the presence of the functional homologue *AlgA*, which may compensate for the *WbpW* deficiency in these mutants. Thus, *WbpW* *AlgA* double mutants were constructed. These mutants also produced low levels of A-band LPS. A search of the PAO1 genome sequence identified a second *AlgA* homologue, designated ORF488, which may be responsible for the synthesis of GDP-D-Man in the absence of *WbpW* and *AlgA*. Polymerase chain reaction (PCR) amplification and sequence analysis of this region reveals three

open reading frames (ORFs), orf477, orf488 and orf303, arranged as an operon. ORF477 is homologous to initiating enzymes that transfer glucose 1-phosphate onto undecaprenol phosphate (Und-P), while ORF303 is homologous to L-rhamnosyltransferases involved in polysaccharide assembly. Chromosomal mapping using pulsed field gel electrophoresis (PFGE) and Southern hybridization places orf477, orf488 and orf303 between 0.3 and 0.9 min on the 75 min map of PA01, giving it a map location distinct from that of previously described polysaccharide genes. This region may represent a unique locus within *P. aeruginosa* responsible for the synthesis of another polysaccharide molecule.

CONTROLLED TERM: Medical Descriptors:  
 article  
 \*bacterial cell wall  
 \*bacterial virulence  
 chromosome map  
     chromosome mutation  
 cystic fibrosis: ET, etiology  
 enzyme activity  
 gene cluster  
 nonhuman  
 \*nucleotide sequence  
 open reading frame  
 operon  
 priority journal  
 protein expression  
 \*Pseudomonas aeruginosa  
 restriction mapping  
     Salmonella enterica  
 sequence analysis  
 sequence homology  
 structure analysis

CONTROLLED TERM: Drug Descriptors:  
 \*alginic acid: EC, endogenous compound  
 bacterial enzyme: EC, endogenous compound  
 \*bacterial polysaccharide: EC, endogenous compound  
 \*bacterium lipopolysaccharide: EC, endogenous compound  
 cell surface marker: EC, endogenous compound  
 gene product: EC, endogenous compound  
 mannose 1 phosphate guanylyltransferase: EC, endogenous compound  
     mannose phosphate isomerase: EC, endogenous compound  
 O antigen: EC, endogenous compound  
 phosphomannomutase: EC, endogenous compound  
 \*rhamnose: EC, endogenous compound  
 RNA precursor: EC, endogenous compound  
 unclassified drug  
 virulence factor: EC, endogenous compound

CAS REGISTRY NO.: (alginic acid) 28961-37-7, 29894-36-8, 9005-32-7, 9005-38-3; (mannose phosphate isomerase) 9023-88-5; (phosphomannomutase) 59536-73-1; (rhamnose) 10485-94-6, 3615-41-6

GENE NUMBER: GENBANK AF009955 submitted number; GENBANK AF009956 submitted number; GENBANK AF053937 submitted number

L138 ANSWER 24 OF 25 EMBASE COPYRIGHT (c) 2010 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1975094782 EMBASE Full-text

TITLE: Relation of lipopolysaccharide character to P1 sensitivity

in *Salmonella typhimurium*.  
 AUTHOR: Ornellas, E.P.; Stocker, B.A.D.  
 CORPORATE SOURCE: Dept. Med. Microbiol., Stanford Univ. Sch. Med., Stanford, Calif. 94305, United States.  
 SOURCE: Virology, (1974) Vol. 60, No. 2, pp. 491-502.  
 ISSN: 0042-6822 CODEN: VIRLAX  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 029 Clinical and Experimental Biochemistry  
 003 Endocrinology  
 004 Microbiology: Bacteriology, Mycology, Parasitology and Virology

LANGUAGE: English

ABSTRACT: Phage Plclr (a variant of Plkc), grown on an LT2 derivative so as to be appropriately modified, was tested for ability to produce plaques on numerous *Salmonella typhimurium* strains of different lipopolysaccharide (LPS) character: the rate of irreversible adsorption of Plclr by representative strains was measured. It appeared that the Pl-resistance of wild type (i.e. smooth) *S. typhimurium* (and of some classes of rough mutant) results from failure to adsorb the phage. Plclr plated efficiently only on the 4 LPS classes which are sensitive to phage C21 and make either galactose deficient (classes galE and rfaH) or glucose deficient incomplete core LPS (classes rfaG and galU). Rates of adsorption  $\geq 40 \times 10^{-11}$ /bacterium/min. were observed only for bacteria unable to make UDPgalactose, either by point mutation at galE or by deletion of the gal operon. A low, variable e.o.p. (usually  $10^{-5}$  to  $10^{-6}$ ) was obtained on mutants making complete core LPS, either without O chains (classes rfb, pmf, and rfaL) or with only single O units (class rfc), and on mutants deficient in addition of the distal heptose unit of the core (class rfaF). Phage Plclr had no detectable effect on smooth strains or mutants with various other LPS core defects. Phage Plcm had the same host range, except that it plated efficiently on some strains on which Plclr plated with low and variable efficiency; it converted some Pl-sensitive strains to chloramphenicol resistance, but the number of resistant colonies obtained was always less than the number of plaques produced. Phage Plclr grown on *E. coli* K12 plated efficiently on galE, etc., derivatives of an LT2 line made restriction negative by mutations at hspLT and hspS, but did not plate (e.o.p.  $< 10^{-3}$ ) on LT2 galE wild type for restriction.

CONTROLLED TERM: Medical Descriptors:  
 \*bacteriophage  
 \*biochemistry  
 \*escherichia coli  
 microorganism  
 \*salmonella typhimurium

CONTROLLED TERM: Drug Descriptors:  
 \*chloramphenicol  
 \*galactose  
 \*glucose  
 \*lipopolysaccharide

CAS REGISTRY NO.: (chloramphenicol) 134-90-7, 2787-09-9, 56-75-7; (galactose) 26566-61-0, 50855-33-9, 59-23-4; (glucose) 50-99-7, 84778-64-3

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ACCESSION NUMBER: 0048099719 EMBASE Full-text  
 TITLE: Haptenic O antigen as a polymeric intermediate of in vivo synthesis of lipopolysaccharide by *Salmonella typhimurium*.  
 AUTHOR: Kent, J.L. (correspondence); Osborn, M.J.  
 CORPORATE SOURCE: Dept. of Mol. Biol., Albert Einstein Coll. of Med., Bronx, NY 10461, United States.

SOURCE: Biochemist, (1968) Vol. 7, No. 12, pp. 4419-4422.  
ISSN: 0954-982X  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: CLASSIC  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: Jun 2010  
Last Updated on STN: Jun 2010

ABSTRACT: A mutant strain of *S. typhimurium* deficient in phosphomannose isomerase was used to study the kinetics of O antigen synthesis in vivo, these polysaccharides being the sole end products of <sup>14</sup>C mannose incorporation. The kinetics of uptake of radioactivity into haptenic O antigen and lipopolysaccharide were consistent with the prediction of an intermediate with high turnover rate. Pulse chase studies demonstrated rapid and efficient transfer of O antigenic radioactivity from antigen carrier lipid hapten to lipopolysaccharide; at least 80% of the label transferred to lipopolysaccharide during the initial chase period was derived from hapten. The addition of completed O antigenic polymer to the preformed lipopolysaccharide acceptor represents a unique biochemical reaction whereby two different polymers are covalently joined.

CONTROLLED TERM: Medical Descriptors:  
kinetics  
mutant  
\*polymerization  
prediction  
pulse rate  
radioactivity  
    \**Salmonella typhimurium*  
\*synthesis  
turnover time

CONTROLLED TERM: Drug Descriptors:  
antigen  
hapten  
lipid  
\*lipopolysaccharide  
mannose  
    mannose phosphate isomerase  
\*O antigen  
polymer  
polysaccharide

CAS REGISTRY NO.: CAS Supplied: (MANNOSE PHOSPHATE ISOMERASE) 9023-88-5;  
(MANNOSE) 3458-28-4Q, 31103-86-3Q

FILE 'HOME' ENTERED AT 10:27:40 ON 30 NOV 2010



## SEARCH HISTORY

=&gt; d his nofile

(FILE 'HOME' ENTERED AT 08:51:48 ON 30 NOV 2010)

FILE 'CAPLUS' ENTERED AT 08:52:04 ON 30 NOV 2010

E US2004-511616/APPS

E US2005-511616/APPS

L1 1 SEA SPE=ON ABB=ON US2005-511616/AP  
D SCA  
D AB  
E CURTISS R/AU

L2 252 SEA SPE=ON ABB=ON CURTISS R/AU OR CURTISS R III/AU OR  
CURTISS RAY III/AU OR CURTISS ROY?/AU

L3 37998 SEA SPE=ON ABB=ON SALMONELLA/CW  
E ARACP/BI

L4 3 SEA SPE=ON ABB=ON ((ARACP OR ARA CP)(W)BAD OR ARACPBAD OR  
ARA CPBAD)/BI

L5 708 SEA SPE=ON ABB=ON GENE#/OBI(L)FUR/OBI OR (FUR GENE#)/BI  
D SCA L4

L6 43 SEA SPE=ON ABB=ON L5 AND L3

L7 51696 SEA SPE=ON ABB=ON ATTENUAT?/OBI

L8 10 SEA SPE=ON ABB=ON L3 AND L5 AND L7  
E LIPOPOLYSACCHARIDE/CT  
E E3+ALL

L9 38618 SEA SPE=ON ABB=ON LIPOPOLYSACCHARIDES/CT

L10 2 SEA SPE=ON ABB=ON L9 AND L6  
D SCA

L11 524 SEA SPE=ON ABB=ON L9(L)SYNTHES?/OBI

L12 1 SEA SPE=ON ABB=ON L11 AND L3 AND L5

L13 4541 SEA SPE=ON ABB=ON O/OBI(L)ANTIGEN#/OBI

L14 238 SEA SPE=ON ABB=ON L13 AND L3 AND L9  
E O ANTIGEN+ALL/CT

L15 3376 SEA SPE=ON ABB=ON O/OBI(L)ANTIGEN#/CW

L16 214 SEA SPE=ON ABB=ON L15 AND L3 AND L9

L17 0 SEA SPE=ON ABB=ON L15 AND L3 AND L9 AND (L4 OR L5)

L18 2 SEA SPE=ON ABB=ON L15 AND L3 AND (L4 OR L5)

L19 3 SEA SPE=ON ABB=ON L11 AND L15 AND L3

L20 12 SEA SPE=ON ABB=ON L3 AND L7 AND L15

L21 6 SEA SPE=ON ABB=ON L3 AND L7 AND L15 AND L9

L22 970 SEA SPE=ON ABB=ON PMI/BI

L23 3 SEA SPE=ON ABB=ON PFUR/BI

L24 0 SEA SPE=ON ABB=ON TTARACP?/BI  
D SCA L23 TI

L25 16 SEA SPE=ON ABB=ON L22 AND L3

L26 1 SEA SPE=ON ABB=ON Δ/BI(W)L22  
D SCA  
E ΔPMI/BI

L27 1 SEA SPE=ON ABB=ON ΔPMI/BI  
D SCA

L28 328337 SEA SPE=ON ABB=ON MUTAT?/OBI OR MUTANT#/OBI

L29 18181 SEA SPE=ON ABB=ON L3(L)TYPHIMURIUM/OBI

L30 12 SEA SPE=ON ABB=ON L22 AND L28 AND L3

L31 10 SEA SPE=ON ABB=ON L22 AND L28 AND L29  
D QUE

L32 9 SEA SPE=ON ABB=ON L22 AND L28 AND L29 AND L7

L33 1 SEA SPE=ON ABB=ON L31 NOT L32  
D SCA

L34 68 SEA SPE=ON ABB=ON L2 AND L3 AND (L4 OR L5 OR L7 OR L9 OR L15  
OR L22 OR L23 OR L28)  
L35 12 SEA SPE=ON ABB=ON L2 AND (L4 OR L8 OR L12 OR L18 OR L19 OR  
L21 OR L23 OR L33)

FILE 'MEDLINE' ENTERED AT 09:10:49 ON 30 NOV 2010

E CURTIIS R/AU  
L36 248 SEA SPE=ON ABB=ON CURTISS R?/AU,AUTH  
E CURTISS R/AU  
L37 48420 SEA SPE=ON ABB=ON SALMONELLA+NT/CT  
L38 1 SEA SPE=ON ABB=ON ((ARACP OR ARA CP)(W)BAD OR ARACPBAD OR  
ARA CPBAD)  
D SCA  
L39 2584 SEA SPE=ON ABB=ON O ANTIGENS/CT  
L40 7659 SEA SPE=ON ABB=ON VACCINES, ATTENUATED/CT  
L41 491950 SEA SPE=ON ABB=ON MUTATION+NT/CT  
L42 11848 SEA SPE=ON ABB=ON MUTANT PROTEINS+NT/CT  
L43 154 SEA SPE=ON ABB=ON FUR GENE#  
D TRIAL 1 50 100 150  
L44 958 SEA SPE=ON ABB=ON PMI OR ΔPMI  
L45 2 SEA SPE=ON ABB=ON PFUR  
L46 0 SEA SPE=ON ABB=ON TTARACP?  
L47 5 SEA SPE=ON ABB=ON L43 AND L37  
L48 171 SEA SPE=ON ABB=ON L39(L)BI/CT  
L49 0 SEA SPE=ON ABB=ON L48 AND L43  
L50 0 SEA SPE=ON ABB=ON L39 AND L43  
L51 5 SEA SPE=ON ABB=ON L37 AND L43  
D SCA  
L52 490 SEA SPE=ON ABB=ON FERRIC UPTAKE REGULATING PROTEINS,  
BACTERIAL/CN  
L53 27 SEA SPE=ON ABB=ON L52 AND L37  
L54 0 SEA SPE=ON ABB=ON L53 AND L39  
L55 1 SEA SPE=ON ABB=ON L52 AND L37 AND L40  
L56 20666 SEA SPE=ON ABB=ON BACTERIAL OUTER MEMBRANE PROTEINS+NT/CT  
L57 1 SEA SPE=ON ABB=ON L52 AND L37 AND L56  
L58 7 SEA SPE=ON ABB=ON L44 AND L37  
D SCA  
L59 262 SEA SPE=ON ABB=ON MANNOSE-6-PHOSPHATE ISOMERASE/CT  
L60 1 SEA SPE=ON ABB=ON L59 AND L37 AND (L40 OR L41 OR L42)  
L61 5 SEA SPE=ON ABB=ON L59 AND L37  
L62 3 SEA SPE=ON ABB=ON L44 AND L37 AND (L40 OR L41 OR L42)  
L63 22571 SEA SPE=ON ABB=ON SALMONELLA TYPHIMURIUM/CT  
L64 4 SEA SPE=ON ABB=ON L63 AND L44  
L65 67 SEA SPE=ON ABB=ON L36 AND L37 AND (L38 OR L39 OR L40 OR L41  
OR L42 OR L43 OR L44 OR L45 OR L52 OR L56 OR L59)  
L66 5 SEA SPE=ON ABB=ON L36 AND L37 AND (L40 OR L41 OR L42) AND  
(L38 OR L39 OR L43 OR L44 OR L45 OR L52 OR L56 OR L59)

FILE 'EMBASE' ENTERED AT 09:30:55 ON 30 NOV 2010

E CURTISS R/AU  
L67 19 SEA SPE=ON ABB=ON CURTISS R?/AU  
L68 67092 SEA SPE=ON ABB=ON SALMONELLA+NT/CT  
L69 25567 SEA SPE=ON ABB=ON SALMONELLA TYPHIMURIUM/CT  
E FERRIC UPTAKE/CT  
L70 367 SEA SPE=ON ABB=ON FERRIC UPTAKE REGULAT?  
L71 190 SEA SPE=ON ABB=ON FUR GENE#  
D TRIAL 1 50 100 190  
L72 41 SEA SPE=ON ABB=ON FUR GENE/CT  
E MANNOSE-6-PHOSPHATE ISOMERASE/CT  
E E3+ALL

L73 325 SEA SPE=ON ABB=ON MANNOSE PHOSPHATE ISOMERASE/CT  
 E PHOSPHATE MANNOSE IS/CT  
 E O ANTIGENS+ALL/CT  
 L74 2711 SEA SPE=ON ABB=ON O ANTIGEN/CT  
 L75 1095 SEA SPE=ON ABB=ON PMI OR ΔPMI OR DELTAPMI  
 L76 4 SEA SPE=ON ABB=ON PFUR  
 L77 3 SEA SPE=ON ABB=ON TTARA?  
 E ATTENUATE/CT  
 E VACCINES, ATTENUATED+ALL/CT  
 E E2+ALL  
 L78 11332 SEA SPE=ON ABB=ON LIVE VACCINE/CT  
 L79 189362 SEA SPE=ON ABB=ON ATTENUAT?  
 E DELTAPFUR  
 E MUTATION+ALL/CT  
 L80 544225 SEA SPE=ON ABB=ON MUTATION+NT/CT  
 E MUTANT/CT  
 E E3+ALL  
 L81 48065 SEA SPE=ON ABB=ON MUTANT/CT OR BACTERIUM MUTANT+NT/CT  
 E MUTANT PRO/CT  
 E E9+ALL  
 L82 31722 SEA SPE=ON ABB=ON MUTANT PROTEIN/CT  
 L83 25 SEA SPE=ON ABB=ON PFUR?  
 L84 1 SEA SPE=ON ABB=ON ((ARACP OR ARA CP) (W)BAD OR ARACPBAD OR  
 ARA CPBAD)  
 L85 7 SEA SPE=ON ABB=ON L68 AND L71  
 L86 10 SEA SPE=ON ABB=ON L68 AND L70 AND (L78 OR L79 OR L80 OR L81  
 OR L82)  
 L87 1 SEA SPE=ON ABB=ON L68 AND L70 AND L74  
 L88 8 SEA SPE=ON ABB=ON L86 NOT (L85 OR L85 OR L87)  
 D SCA  
 L89 11319 SEA SPE=ON ABB=ON REGULATOR GENE/CT  
 L90 1 SEA SPE=ON ABB=ON L86 AND L89  
 L91 0 SEA SPE=ON ABB=ON L77 AND L83  
 L92 0 SEA SPE=ON ABB=ON L68 AND (L77 OR L83)  
 D SCA L77  
 D SCA L76  
 L93 5 SEA SPE=ON ABB=ON L73 AND L68  
 L94 9 SEA SPE=ON ABB=ON L75 AND L68  
 L95 5 SEA SPE=ON ABB=ON L69 AND L75  
 L96 5 SEA SPE=ON ABB=ON L75 AND L68 AND (L78 OR L79 OR L80 OR L81  
 OR L82)  
 L97 9 SEA SPE=ON ABB=ON L67 AND L68 AND (L70 OR L71 OR L72 OR L73  
 OR L74 OR L75 OR L76 OR L77 OR L78 OR L79 OR L80 OR L81 OR L82  
 OR L83 OR L84)

FILE 'STNGUIDE' ENTERED AT 09:47:31 ON 30 NOV 2010

FILE 'PASCAL, BIOTECHNO, WPIX, BIOSIS, DISSABS, LIFESCI, ESBIODBASE,  
 BIOTECHDS, BIOENG, SCISEARCH' ENTERED AT 09:52:46 ON 30 NOV 2010

L98 1063 SEA SPE=ON ABB=ON CURTISS R/AU OR CURTISS R III/AU OR  
 CURTISS ROY?/AU  
 L99 249856 SEA SPE=ON ABB=ON SALMONELLA  
 L100 8 SEA SPE=ON ABB=ON ((ARACP OR ARA CP) (W) BAD OR ARACPBAD OR  
 ARA CPBAD)  
 L101 1088 SEA SPE=ON ABB=ON FUR GENE#  
 L102 1719 SEA SPE=ON ABB=ON FERRIC UPTAKE REGULAT?  
 L103 13365 SEA SPE=ON ABB=ON O(W) ANTIGEN#  
 L104 2667600 SEA SPE=ON ABB=ON MUTAT? OR MUTANT#  
 L105 965 SEA SPE=ON ABB=ON MANNOSE(1A) PHOSPHATE ISOMERASE  
 L106 5259 SEA SPE=ON ABB=ON PMI OR ΔPMI OR DELTAPMI

```

L107      83 SEA SPE=ON  ABB=ON  PFUR? OR DELTAPFUR?
L108      4 SEA SPE=ON  ABB=ON  TTARA?
L109     751214 SEA SPE=ON  ABB=ON  ATTENUAT?
L110     2667600 SEA SPE=ON  ABB=ON  MUTAT? OR MUTANT#
L111      8 SEA SPE=ON  ABB=ON  L99 AND L100
L112     173 SEA SPE=ON  ABB=ON  L99 AND (L101 OR L102)
L113      4 SEA SPE=ON  ABB=ON  L103 AND L112
L114     101 SEA SPE=ON  ABB=ON  L112 AND (L104 OR L109)
L115     89324 SEA SPE=ON  ABB=ON  OUTER MEMBRANE
L116      7 SEA SPE=ON  ABB=ON  L99 AND (L101 OR L102) AND (L104 OR L109)
      AND L115
L117      0 SEA SPE=ON  ABB=ON  L107 AND L108
L118     48 SEA SPE=ON  ABB=ON  (L105 OR L106) AND L110 AND L99
L119     30 DUP REM L118 (18 DUPLICATES REMOVED)
      ANSWERS '1-2' FROM FILE PASCAL
      ANSWERS '3-4' FROM FILE BIOTECHNO
      ANSWERS '5-16' FROM FILE WPIX
      ANSWERS '17-19' FROM FILE BIOSIS
      ANSWERS '20-21' FROM FILE DISSABS
      ANSWERS '22-24' FROM FILE LIFESCI
      ANSWERS '25-26' FROM FILE ESBIODBASE
      ANSWERS '27-28' FROM FILE BIOTECHDS
      ANSWERS '29-30' FROM FILE SCISEARCH
L120     100416 SEA SPE=ON  ABB=ON  L99(W) TYPHIMURIUM
L121      34 SEA SPE=ON  ABB=ON  (L105 OR L106) AND L110 AND L120
L122     22 DUP REM L121 (12 DUPLICATES REMOVED)
      ANSWER '1' FROM FILE PASCAL
      ANSWER '2' FROM FILE BIOTECHNO
      ANSWERS '3-9' FROM FILE WPIX
      ANSWERS '10-12' FROM FILE BIOSIS
      ANSWER '13' FROM FILE DISSABS
      ANSWERS '14-16' FROM FILE LIFESCI
      ANSWERS '17-18' FROM FILE ESBIODBASE
      ANSWERS '19-21' FROM FILE BIOTECHDS
      ANSWER '22' FROM FILE SCISEARCH
      D QUE
L123     13465 SEA SPE=ON  ABB=ON  L110(S)((L106 OR L105 OR L120))
L124      31 SEA SPE=ON  ABB=ON  L121 AND L123
L125     53 SEA SPE=ON  ABB=ON  L98 AND L99 AND (L104 OR L109) AND (L100
      OR L101 OR L102 OR L103 OR L105 OR L106 OR L107 OR L108 OR
      L115)
L126     29 SEA SPE=ON  ABB=ON  L98 AND L120 AND (L104 OR L109) AND (L100
      OR L101 OR L102 OR L103 OR L105 OR L106 OR L107 OR L108 OR
      L115)
L127     21 DUP REM L126 (8 DUPLICATES REMOVED)
      ANSWERS '1-3' FROM FILE PASCAL
      ANSWERS '4-7' FROM FILE WPIX
      ANSWERS '8-18' FROM FILE BIOSIS
      ANSWER '19' FROM FILE BIOTECHDS
      ANSWERS '20-21' FROM FILE SCISEARCH

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FILE 'STNGUIDE' ENTERED AT 10:01:47 ON 30 NOV 2010

FILE 'PASCAL, BIOTECHNO, WPIX, BIOSIS, DISSABS, LIFESCI, ESBIODBASE,  
BIOTECHDS, BIOENG, SCISEARCH' ENTERED AT 10:02:44 ON 30 NOV 2010  
D QUE L126

FILE 'CAPLUS' ENTERED AT 10:02:44 ON 30 NOV 2010  
D QUE L35

FILE 'MEDLINE' ENTERED AT 10:02:44 ON 30 NOV 2010  
D QUE L66

FILE 'EMBASE' ENTERED AT 10:02:44 ON 30 NOV 2010  
D QUE L97

FILE 'MEDLINE, CAPLUS, PASCAL, WPIX, BIOSIS, LIFESCI, BIOTECHDS, SCISEARCH, EMBASE' ENTERED AT 10:02:45 ON 30 NOV 2010

L128           39 DUP REM L66 L35 L126 L97 (16 DUPLICATES REMOVED)  
                  ANSWERS '1-5' FROM FILE MEDLINE  
                  ANSWERS '6-14' FROM FILE CAPLUS  
                  ANSWER '15' FROM FILE PASCAL  
                  ANSWER '16' FROM FILE WPIX  
                  ANSWERS '17-27' FROM FILE BIOSIS  
                  ANSWER '28' FROM FILE BIOTECHDS  
                  ANSWERS '29-30' FROM FILE SCISEARCH  
                  ANSWERS '31-39' FROM FILE EMBASE  
                  D IALL 1-5  
                  D IBIB ABS HITIND 6-14  
                  D IALL 15  
                  D IFULL 16  
                  D IALL 17-39

FILE 'STNGUIDE' ENTERED AT 10:03:36 ON 30 NOV 2010

FILE 'PASCAL, BIOTECHNO, WPIX, BIOSIS, DISSABS, LIFESCI, ESBIODBASE, BIOTECHDS, BIOENG, SCISEARCH' ENTERED AT 10:05:33 ON 30 NOV 2010

                  D QUE L111  
                  D QUE L113  
                  D QUE L116  
L129           12 SEA SPE=ON   ABB=ON   (L111 OR L113 OR L116) NOT L126

FILE 'CAPLUS' ENTERED AT 10:05:37 ON 30 NOV 2010

                  D QUE L4  
                  D QUE L8  
                  D QUE L12  
                  D QUE L18  
                  D QUE L19  
                  D QUE L21  
L130           10 SEA SPE=ON   ABB=ON   (L4 OR L8 OR L12 OR L18 OR L19 OR L21) NOT  
                  L35

FILE 'EMBASE' ENTERED AT 10:05:39 ON 30 NOV 2010

                  D QUE L84  
                  D QUE L85  
                  D QUE L87  
                  D QUE L90  
L131           10 SEA SPE=ON   ABB=ON   (L84 OR L85 OR L87 OR L90) NOT L97

FILE 'MEDLINE' ENTERED AT 10:05:41 ON 30 NOV 2010

                  D QUE L38  
                  D QUE L47  
                  D QUE L50  
                  D QUE L54  
                  D QUE L55  
                  D QUE L57  
L132           5 SEA SPE=ON   ABB=ON   (L38 OR L47 OR L55 OR L57) NOT L66

FILE 'STNGUIDE' ENTERED AT 10:05:51 ON 30 NOV 2010

FILE 'MEDLINE, CAPLUS, WPIX, BIOSIS, ESBIODBASE, BIOTECHDS, SCISEARCH, EMBASE' ENTERED AT 10:06:06 ON 30 NOV 2010

L133 27 DUP REM L132 L130 L129 L131 (10 DUPLICATES REMOVED)  
 ANSWERS '1-5' FROM FILE MEDLINE  
 ANSWERS '6-15' FROM FILE CAPLUS  
 ANSWER '16' FROM FILE WPIX  
 ANSWERS '17-19' FROM FILE BIOSIS  
 ANSWER '20' FROM FILE BIOTECHDS  
 ANSWERS '21-25' FROM FILE SCISEARCH  
 ANSWERS '26-27' FROM FILE EMBASE  
 D IALL 1-5  
 D IBIB ABS HITIND 6-15  
 D IFULL 16  
 D IALL 17-27

FILE 'STNGUIDE' ENTERED AT 10:06:43 ON 30 NOV 2010

FILE 'PASCAL, BIOTECHNO, WPIX, BIOSIS, DISSABS, LIFESCI, ESBIODBASE, BIOTECHDS, BIOENG, SCISEARCH' ENTERED AT 10:26:30 ON 30 NOV 2010

D QUE L117  
 D QUE L124  
 L134 21 SEA SPE=ON ABB=ON L124 NOT (L129 OR L126)

FILE 'CAPLUS' ENTERED AT 10:26:35 ON 30 NOV 2010

D QUE L24  
 D QUE L23  
 D QUE L33  
 L135 4 SEA SPE=ON ABB=ON (L23 OR L33) NOT (L130 OR L35)

FILE 'EMBASE' ENTERED AT 10:26:36 ON 30 NOV 2010

D QUE L91  
 D QUE L92  
 D QUE L93  
 D QUE L95  
 D QUE L96  
 L136 11 SEA SPE=ON ABB=ON (L93 OR L95 OR L96) NOT (L131 OR L97)

FILE 'MEDLINE' ENTERED AT 10:26:38 ON 30 NOV 2010

D QUE L46  
 D QUE L45  
 D QUE L61  
 D QUE L62  
 D QUE L64  
 L137 10 SEA SPE=ON ABB=ON (L45 OR L61 OR L62 OR L64) NOT (L132 OR L66)

FILE 'STNGUIDE' ENTERED AT 10:26:46 ON 30 NOV 2010

FILE 'MEDLINE, CAPLUS, PASCAL, BIOTECHNO, WPIX, BIOSIS, DISSABS, LIFESCI, ESBIODBASE, BIOTECHDS, SCISEARCH, EMBASE' ENTERED AT 10:27:06 ON 30 NOV 2010

L138 25 DUP REM L137 L135 L134 L136 (21 DUPLICATES REMOVED)  
 ANSWERS '1-10' FROM FILE MEDLINE  
 ANSWERS '11-12' FROM FILE CAPLUS  
 ANSWERS '13-15' FROM FILE WPIX  
 ANSWER '16' FROM FILE BIOSIS  
 ANSWER '17' FROM FILE DISSABS  
 ANSWER '18' FROM FILE LIFESCI  
 ANSWER '19' FROM FILE ESBIODBASE  
 ANSWER '20' FROM FILE BIOTECHDS

ANSWER '21' FROM FILE SCISEARCH  
ANSWERS '22-25' FROM FILE EMBASE  
D IALL 1-10  
D IBIB ABS HITIND 11-12  
D IFULL 13-15  
D IALL 16-25

FILE 'HOME' ENTERED AT 10:27:40 ON 30 NOV 2010

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